Republic of Iraq
Ministry of Higher Education
and Scientific Research
University of Babylon
College of science for women
Department of Chemistry

Synthesis and Characterization a New of 1,3-Oxazepane-4,7-Dione via Schiff base based on 6-aminopenicillanic Acid and it is chelating ability

A Thesis

Submitted to the Council of the College of science for women, University of Babylon as a Partial Fulfillment of the Requirements for the Degree of Master of Science in Chemistry

By

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Supervised by

Asst. Prof. Dr: Sadiq Abdul Hussein Karim

Prof. Dr: Mohammed Hamid Said

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"بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ"

۞ وَلَقَدْ كَرَّمْنَا بَنِي آدَمَ وَحَمَلْنَاهُمْ فِي الْبَرِّ وَالْبَحْرِ وَرَزَقْنَاهُم مِّنَ الطَّيِّبَاتِ وَفَضَّلْنَاهُمْ عَلَىٰ كَثِيرٍ مِّمَّنْ خَلَقْنَا تَفْضِيلًا (70)

صدق الله العلي العظيم

سورة الآسراء- الاية ﴿70﴾

Dedication

To the one who honored me by bearing his name...my father

To the one who taught me the first step..... Mom

To the back, upper arm, and forearm..... my husband

To the adornment and joy of my life.... my children

To those who left us in a hurry without saying goodbye...my brother (may God have mercy on him)

To the light of my eyes and the light of my path..... my brother and sisters

To all the family and friends

To my respected teachers

To everyone who taught me a letter

To everyone who supported me, even with a smile

I dedicate to you the fruit of my labor and effort with love, elevation and dignity

Mays

Acknowledgments

Praise be to ***Allah***, Lord of the worlds. Praise be to ***Allah***, who helped me and gave me the strength, to complete this thesis.

I would like to extend my special thanks and appreciation to my supervisor, ***Asst. Prof. Dr: Sadiq A. Karim, Prof. Dr. Mohammed Hamid said*** for his suggestion and for providing his continuous advice and valuable guidance, without his guidance and close supervision of the work, when it is never achieved.

I also express my thanks and gratitude to the deanship of the college of science for women and the head of the department of chemistry***, Asst. Prof. Dr. Hazim Al- Jeboree***, and all my professors who helped me and provided their valuable pieces of advice.

I also would like to extend my sincere thanks and appreciation to ***Dr. Ali Talb and Prof. Dr. Hasanian Khaleel*** for their help in this work.

Finally, I would like to express my sincere thanks and appreciation to the members of my family and my husband, who has been of help to me and a support throughout this period me until I reached this stage.

Mays

Supervisor's Certification

I, certify that this research entitled **" Synthesis and Characterization a New of 1,3-Oxazepane-4,7-Dione via Schiff base based on 6-aminopenicillanic Acid and it is chelating ability "** was prepared by **" Mays Said Obaid "** under my supervision at the Department of Chemistry/ College of Science for women /University of Babylon as a partial fulfillment of the requirements for the Degree of Master in Science / Chemistry.

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Date: / 6 / 2022

Recommendation of Head of Chemistry Department

According to the available recommendation , I forward this thesis for Discussion

Signature of Chemistry Department

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Address : Head of Chemistry Department

University of Babylon / College of Science for Woman

Date: / 6 / 2022

Summary

Five ligands have been prepared work by the reaction of 6-aminopenicillanic acid (6-APA) with (n-Butylaldehyde, Crotonaldehyde, Terephthalaldehyde, Furfuraldehyde,Benzaldehyde) to produce L1, L2,L3,L4 and L5 respectively. Four new complexes have been synthesized by the reaction of the above derivative ligands with metal ions Zn (II), that L1, L2, and L4 interacted with these metal ions in mole ratio [1:2] metal to ligand [M: L] respectively, but L3 in mole ratio [1:1] metal to ligand.

As well as, synthesized 1,3-oxazepine derivatives by the reaction Schiff bases with (succinic anhydride, phthalic anhydride and maleic anhydride) to give seven-membered heterocyclic ring derivatives (C1,C2,C3,C4,C5,C6,C7,C8,C9), and by the reaction of the above derivative with metal ions Zn (II), Produces nine new complexes (D1,D2,D3,D4,D5,D6,D7,D8,D9).The structure formula of these compounds were confirmed by using Melting Points, FT-IR, (^{1}H and ^{13}C) NMR spectroscopy, Atomic Absorption, Mass Spectrometric, The synthesized compounds were screened for their antibacterial activity against bacteria gram negative (*Pseudomonas)* and gram positive *(Staphylococcus aureus*), The Schiff bases, 1,3-oxazepine derivatives and its complexes were discovered to have excellent inhibitory action against bacteria (*Pseudomonas and Staphylococcus aureus*). As a consequence, the compounds developed might be viable alternatives for commonly used medications.

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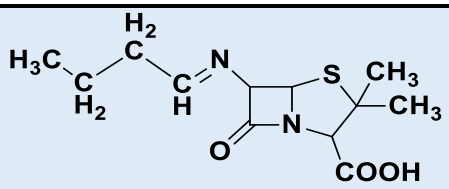
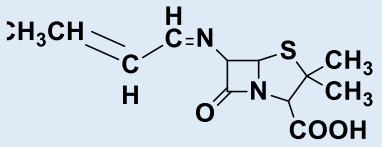
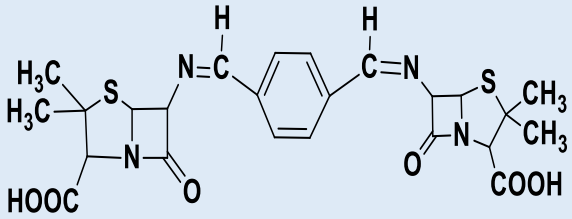
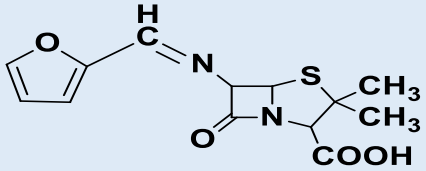
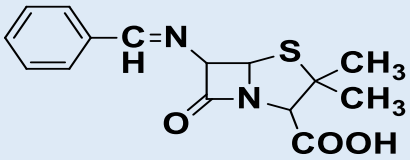
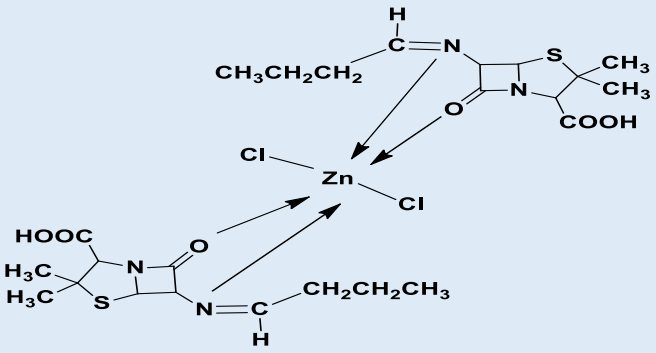
List of abbreviations

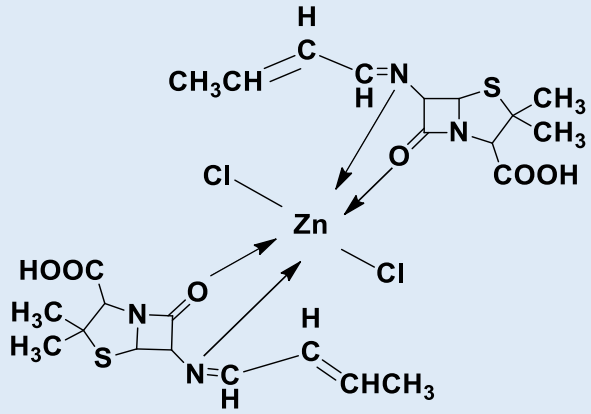
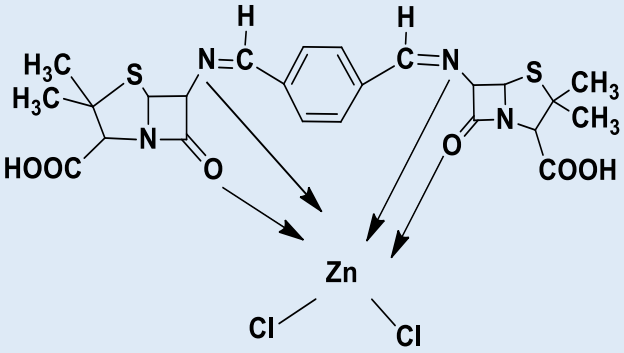
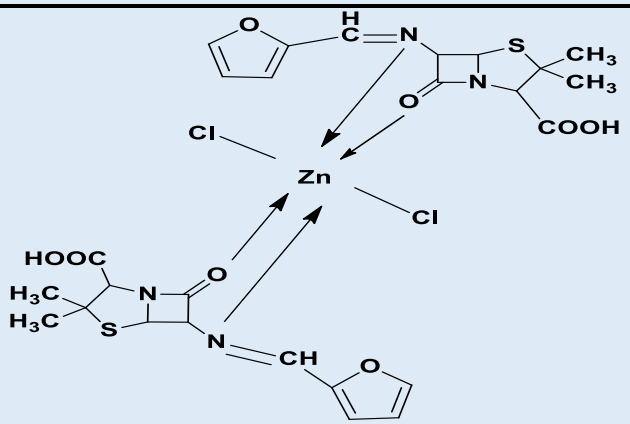
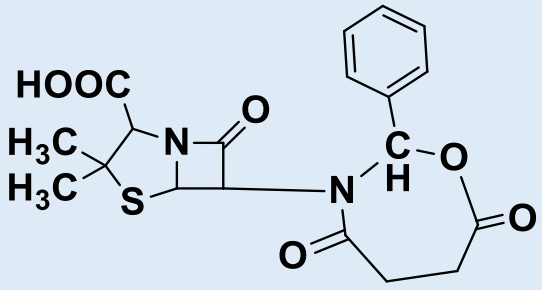
Shorten	Full name
λ_{max}	Maximum wavelength

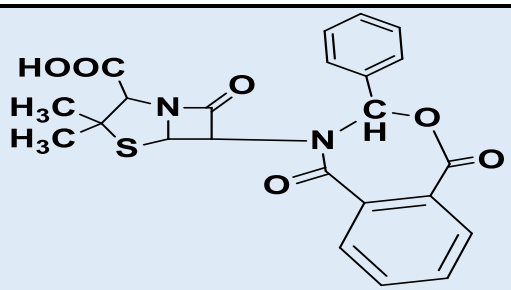
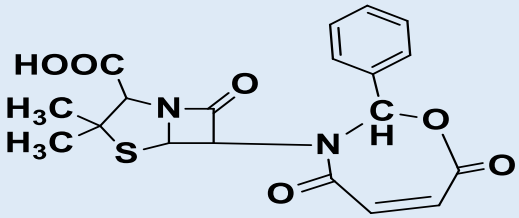
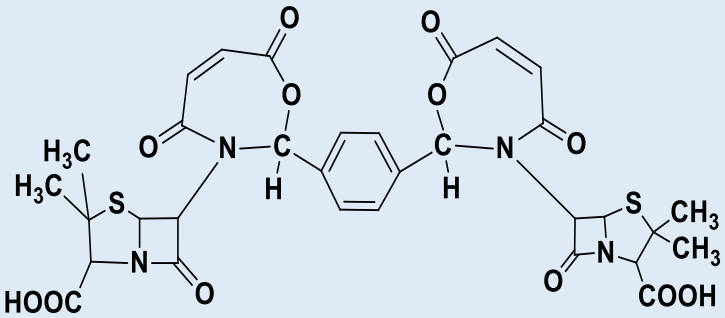
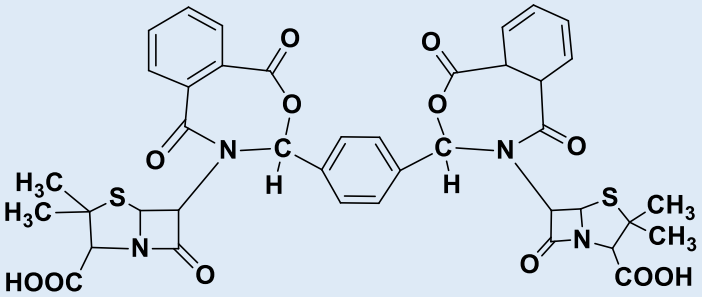
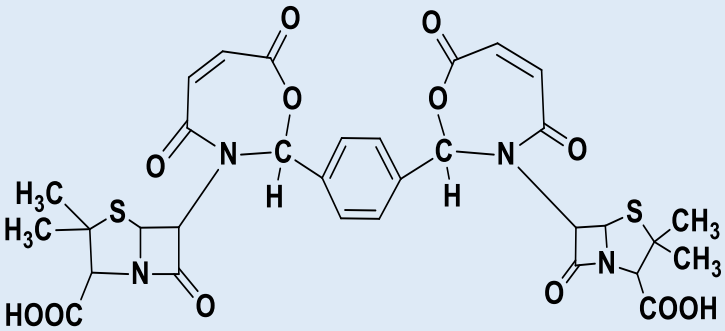
Shorten	Full name
6APA	6-aminopenicillanic acid
DMSO	Dimethyl sulfoxide
Oct	Octahedral
β-lactam	Beta Lactam
M.P	Melting point
^{1}HNMR	Proton-Nuclear Magnetic Resonance
^{13}CNMR	Carbon 13- Nuclear Magnetic Resonance
FT-IR	Fourier Transform Infrared
UV–Vis	Ultraviolet-Visible Spectroscopy
nm	Nanometer
PAA	Phenyl Acetic Acid
PGA	Penicillin G acylase
TNT	tetra-nitro toluene
CNS	Central Nervous system

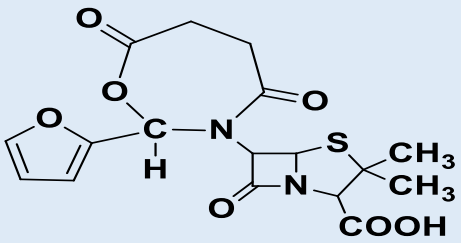
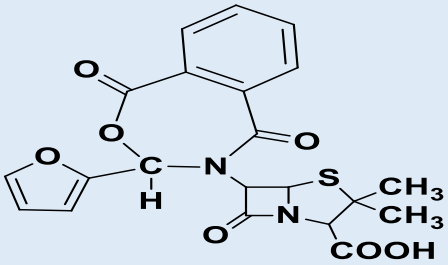
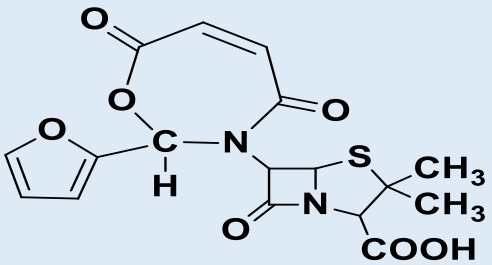
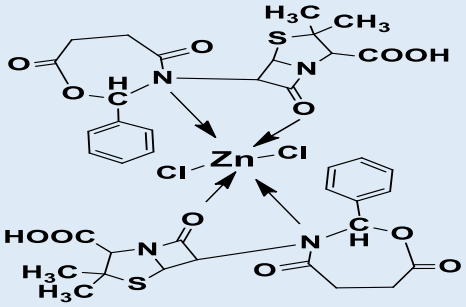
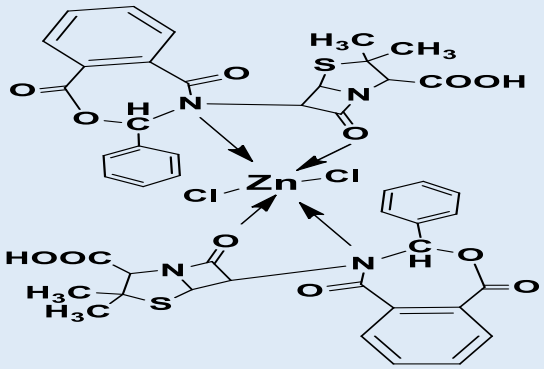
Table of Molecules

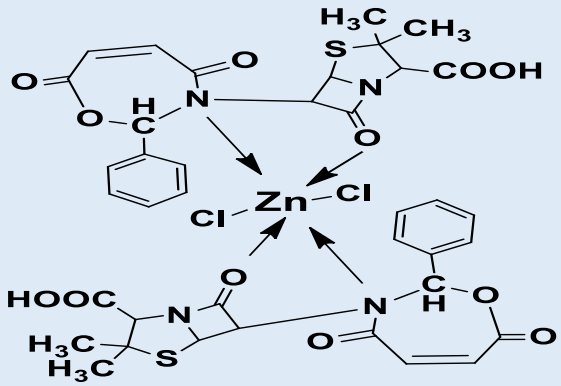
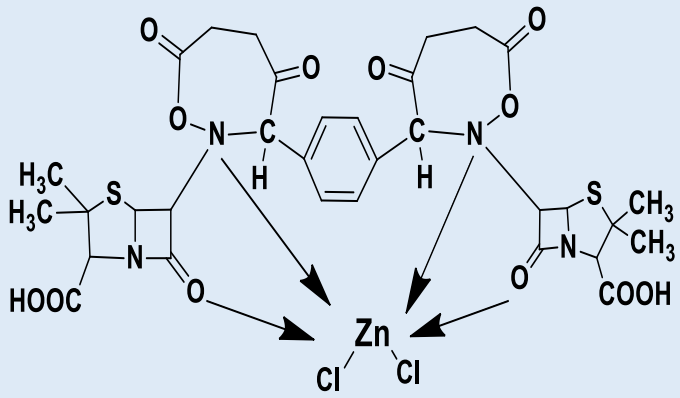
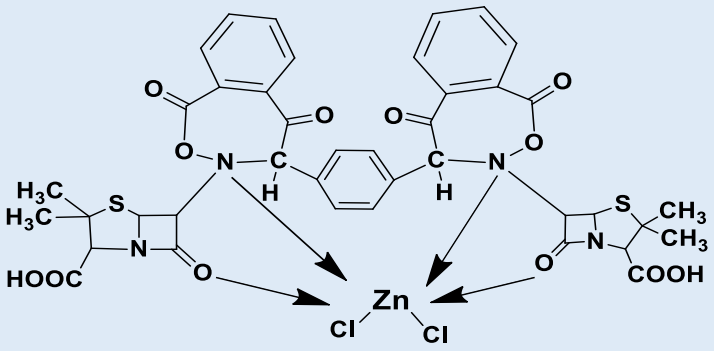
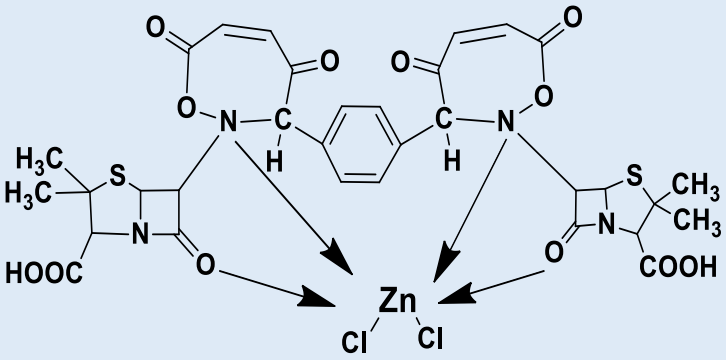
Code	Chemical Name	Structure

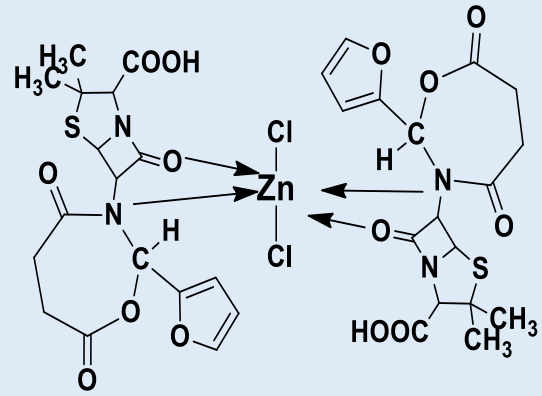
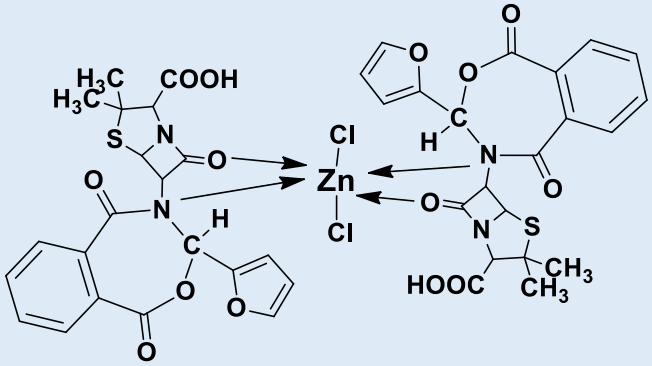
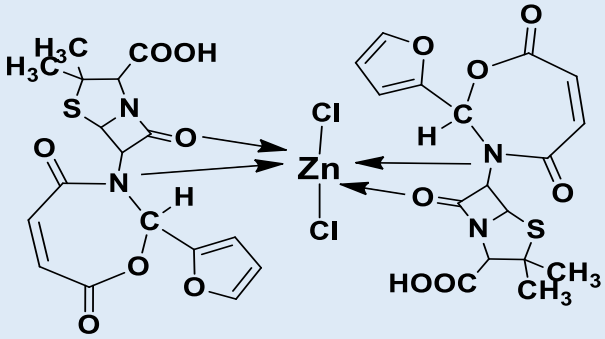
L1	**6-(butylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid**	
L2	**6-(but-2-1-ylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid**	
L3	**6,6'-((1,4-phenylenebis (methaneylylidene))bis (azaneylylidene))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid)**	
L4	**6-((furan-2-ylmethylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid**	
L5	**6-(benzylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid**	
B1	**[bis (6-(butylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid)dichloro zinc(II)]**	

B2	**[bis(6-(but-2-1-ylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid)dichloro zinc(II)]**	
B3	**[(6,6'-((1,4-phenylenebis (methaneylylidene))bis (azaneylylidene))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid) dichlorozinc(II)]**	
B4	**[bis(6-((furan-2-ylmethylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid) dichlorozinc(II)]**	
C1	**6-(4,7-dioxo-2-phenyl-1,3-oxazepan-3-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0]heptane-2-carboxylic acid**	
	6-(1,5-dioxo-3-phenylbenzo[e][1,3]oxazepin-	

C2	**4(*1H,3H,5H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid**	
C3	**6-(4,7-dioxo-2-phenyl-1,3-oxazepin-3(*2H,4H,7H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid**	
C4	**6,6'-(2,2'-(1,4-phenylene) bis(4,7-dioxo-1,3-oxazepane-3,2-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0]heptane-2-carboxylic acid)**	
C5	**6,6'-(3,3'-(1,4-phenylene)bis(1,5-dioxobenzo[e][1,3]oxazepine-4,3(*1H,3H,5H*)-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid)**	
C6	**6,6'-(2,2'-(1,4-phenylene)bis(4,7-dioxo-1,3-oxazepine-3,2(2H,4H,7H)-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid)**	

C7	**6-(2-(furan-2-yl)-4,7-dioxo-1,3-oxazepan-3-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid**	
C8	**6-(3-(furan-2-yl)-1,5-dioxobenzo [e][1,3]oxazepin-4(1*H*,3*H*,5*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid**	
C9	**6-(2-(furan-2-yl)-4,7-dioxo-1,3-oxazepin-3(*2H,4H,7H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid**	
D1	**[(4,7-dioxo-2-phenyl-1,3-oxazepan-3-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid) dichlorozinc(II)]**	
D2	**(6-(1,5-dioxo-3-phenylbenzo[e] [1,3]oxazepin -4(1*H*,3*H*,5*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid) dichlorozinc(II)]**	

D3	**[((4,7-dioxo-2-phenyl-1,3-oxazepin-3(2*H*,4*H*,7*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) dichlorozinc(II)]**	
D4	**[(6,6'-(2,2'-(1,4-phenylene)bis(4,7-dioxo-1,3-oxazepane-3,2-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid)) dichlorozinc(II)]**	
D5	**[(5.6,6'-(3,3'-(1,4-phenylene)bis(1,5-dioxobenzo[e][1,3]oxazepine-4,3 (1*H*,3*H*, 5*H*)-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid)) dichlorozinc(II)]**	
D6	**[(6,6'-(2,2'-(1,4-phenylene)bis(4,7-dioxo-1,3-oxazepine-3,2(2*H*,4*H*,7*H*)-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) dichlorozinc(II)]**	

D7	**[(6-(2-(furan-2-yl)-4,7-dioxo-1,3-oxazepan-3-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid) dichlorozinc(II)]**	
D8	**[(6-(3-(furan-2-yl)-1,5-dioxobenzo[e] [1,3]oxazepin-4(1*H*,3*H*,5*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0]heptane-2-carboxylicacid) dichlorozinc(II)]**	
D9	**[(6-(2-(furan-2-yl)-4,7-dioxo-1,3-oxazepin-3(2*H*,4*H*,7*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid) dichlorozinc(II)]**	

Chapter One

Introduction

1- Introduction

1.1-Schiff bases

Schiff bases are derived from an amine and a carbonyl compound, and they were first reported in 1864 the German scientist that called Hugo Schiff [Ashraf, Muhammad Aqeel, *et.al.*,2011]. The azomethine group with the overall formula $RHC=NR_1$, where R and R_1 are aryl, cyclo alkyl, alkyl, or heterocyclic groups that may be exchanged in various ways, gives these compounds their corporate structural property Schiff bases [Enbarai ,*et,al.*,2021],[Spichiger.Keller,*et.al.*,2008]. Commonly known as azomethines, imines, or anils are a type of Schiff base. Several investigations have shown that the presence of a single pair of electrons in a sp^2 hybridized orbital of the nitrogen atom of the imines cluster has biological and chemical significance (which varies depending on the type of substituent on the aromatic rings), because of the relative ease with which artificial flexibility, preparation, and the various aspects of Schiff bases with the C=N group are often used as chelating, mediators[Spichiger.Keller,*et.al.*,2008]. Especially when a functional cluster such as –SH or –OH is present near the azomethine group to form a five- or six-membered ring with the metal ion. The versatility of Schiff base ligands, as well as the analytical, biological, and manufacturing applications of their complexes, necessitates more research in this area. The investigation playing field for Schiff base coordination chemistry has expanded dramatically in recent years.The importance of schiff base complexes in biomedical applications,catalysis,bioinorganic chemistry and science materials,supramolecular chemistry,separation and encapsulation processes, and the formation of composites with unusual properties and

configurations has been well documented and investigated [Mohammed abd *et.al*.,2015]. The (N=CH) (imine) cluster describes these compounds and is important in describing the transamination mechanis reaction in,biologicasystems[K.Y.Lau,*et.al.*,1999][Mohammed abd *et.al.*, 2015].The application of these compounds as an active component is a remarkable use of these compounds. corrosion inhibitor, which is based on their capacity to create a crystalline structure in a short period of time. Schiff bases play an important role in aldehydes, however this is most likely due to the (C=N) bond. In many circumstances, more powerfully [Farag, Ahmed.,*et.al*.,2015].

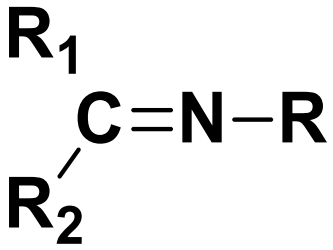


Figure 1.1: Structure of Schiff base

It is obvious from the literature that the study of Schiff base ligand complexes are tied to a number of significant advancements in the field of chemistry.Chemistry of inorganic substances[S.Hazra,*et.al*.,2009 ,M.Asadi,*et.al.*,2010]They were essential in the advancement of new technologies. chemistry of coordination [A.Burkhardt,*et.al.*,2008]. R, R_1, R_2 denotes a phenyl or alkyl group, indicating that the Schiff bases are stable imines. The imine nitrogen and other groups connected to the Schiff base allow these compounds to coordinate with metal ions. They are referred to as "privileged ligands" because the active groups in these compounds can be customized to meet specific needs. Chemists now

create well-designed bridging Schiff bases, which are depicted in the diagram below.

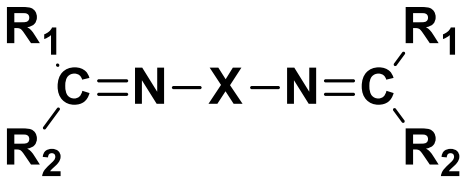


Figure 1.2: Schiff base coordinate with metal ions

Where R_1= H or alkyl group, R_2= phenyl or substituted phenyl group and X= an alkyl or phenyl group [Sarker,Dipta,*et.al.*,2020] .

1.1.1-Types of Schiff bases based on chelating property

-Bidentate Schiff base ligand with O, N donors[S. A. Owolabi. 2014]

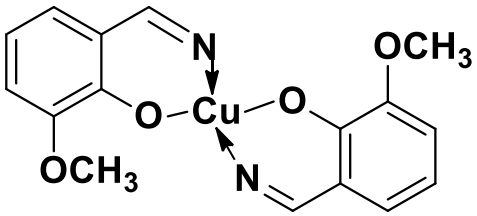


Figure 1.3: Bidentate Schiff base ligand

- Tridentate Schiff base ligand with O, N, Ndonors [R.B.Xu. *et.al.*2008]

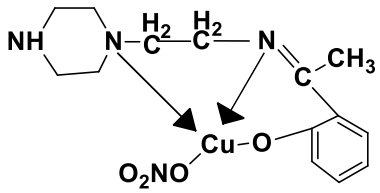


Figure 1.4: Tridentate Schiff base ligand

- Tridentate Schiff base ligand with O, N, N donors [T.Sedaghat, *et, al.*2009]

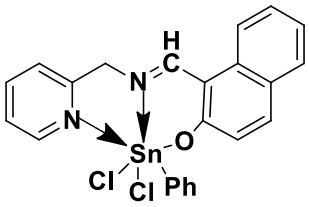


Figure 1.5: Tridentate Schiff base ligand

- Tridentate Schiff base ligand with O, N, S donors[R.J.Yadav,et.al.,2010]

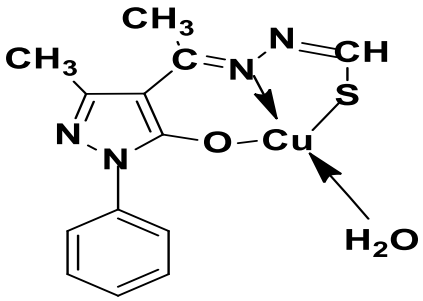


Figure 1.6: Tridentate Schiff base ligand

-Tetra dentate Schiff base ligands with O, N, N, O donors [Joseph .V.A.*et .al*.,2016]

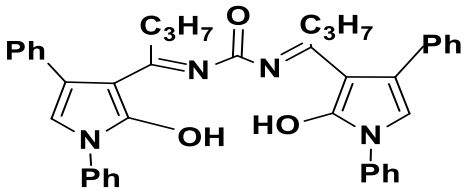


Figure 1.7: Suggested structure of the Schiff base ligand

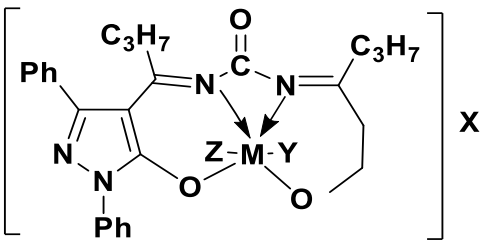


Figure 1.8: Suggested structure of the metal complexes with ONNO donor Schiff base

-Hexa-dentate with N,N,N,N,N,N donors [R.Kannappan,et.al.,2006] [Creaven,BernadetteS.,*et.al*.,2010]

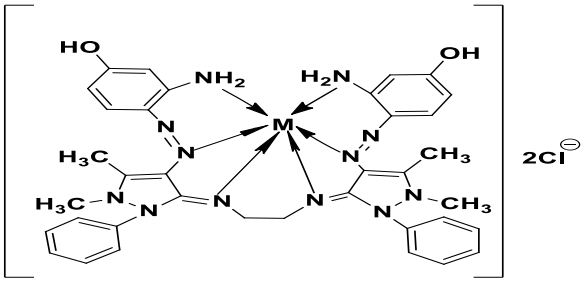


Figure1.9: Hexa-dentate Schiff base ligand

1.1.2-Applications of Schiff bases and their metal complexes

Schiff bases and their metal complexes play an essential role in a variety of biological systems, as well as polymers, colors, medicine, agriculture, and industry. They're also employed as separation or analytical reagents. The principal uses and applications of several Schiff bases and their metal complexes are discussed in this section [A.A.Salih ,*et.al*. 2011,M.S.Mohamad.2013].

1.1.2.1-Antibacterial activity

The Schiff base and its tin complexes of indoline-2,3-dione and 2-amino benzoic acid showed antibacterial activity against S. aureus. When compared to the standard medicine (imipinem), the results showed that the compounds were active, although not as much as the standard drug. The presence of a hydroxyl and phenyl group must be responsible for this activity. The coordination and polarity of a tin (IV) atom with oxygen in the ligand may be responsible for the enhanced activity of organotin complexes[Leite-Sampaio.*et.al*.,2021]. Antibacterial activity was observed in amino acid Schiff bases generated from 2-hydroxy-5-

methylacetaphenone and glycine, as well as their transition metal complexes,Under identical experimental settings,metal complexes showed more activity against the same organism than free ligand, and this increased activity can be explained using chelation theory [Lin,Ying-Chuan,*et,al*2013].. Tetra and hexa-coordinate metal chelate complexes of phosphate Schiff base ligands were found to possess remarkable antibacterial properties but biological activities get enhanced in complexation with metal ions [Vaidya,Atman,*et.al*.,2018].

1.1.2.2-Antifungal activity

Many Schiff bases and their metal complexes have antifungal action, which is stronger in complexes than ligands. Antifungal activity of N-(2-hydroxy-1-nephthalidine phenyl glycine and its transition metal complexes, for example, was investigated, and it was discovered that, when compared to the free ligand, the metal complexes had better antifungal activity [S.Chandra,*et.al*.,2005].

1.1.2.3-Antiviral activity

Gossypol Schiff bases have a significant antiviral activity[Malinowsky,Katharina,*et.al*.,2012].Cucumber mosaic virus is inhibited by silver complexes in oxidation state +1 [F.Meng,*et.al*.,2003]. Ag(I) was found to be effective against cucumber mosaic virus in up to 74.7 percent of cases [Kotadiya,.*et.al.*,2020].

1.1.3-Therapeutic applications

Several Schiff bases have been reported to have anti-inflammatory radical-scavenging analgesic and anti-oxidative properties [Shih,Kuei-Chung,*et.al*.,2014,X.Luo,*et.al*.,2002].Schiff bases generated from thiazole have anti inflammatory and analgesic properties.[Naik.Bis

wajit.*et.al.*,2020].Antioxidant activities of chitosan and carboxymethyl.ch itosan,such as superoxide and hydroxyl scavenging[Kumar,Satish,et.al.,2 015].The metal complexes of furan semicarbazones have anthelmintic a- nd analgesic properties,[Hassan,AliMostafa,*et.al.*,2020.Some Schiff bases and their metal complexes have antitumor and cytotoxic effects. Salicylidieneanthranilic acid has antiulcer action, and when it is complexed with Cu, the antiulcer activity increases[Chan,Yuk-Shing,*et.al.*,2011]. Antitumor action was discovered in Schiff bases made from salicyladehyde, 2,4-dihydroxy-bezaldehyde-glycine, and L-alanine, as well as their metal complexes comprising Cu, Ni, Zn, and Co. Ni has the most activity, followed by Cu,Zn,andCo,with activity varied depending on the metal,according to Schiff[Guerraoui,Abdenour,*et.al.*,20 20] There is no alteration to the base. The activity of amino Schiff bases generated from aromatic and heterocyclic amines against human tumor cell lines is high[Qin,Wenling,*et.,al.*,2013].

1.1.4-Industrial applications

In the dye and polymer sectors, Schiff bases are thought to play a function,Chromium methane compounds [Chovatiya,*et,al.*,2016] and cobalt Schiff base complexes [M Hassan,Ali,*et.al.*,2020] have been used to color leather, food packaging, and wool. To color cellulose polyester fabrics, metal compounds containing the azo group are utilized [Abu-Dief,AhmedM,*et.al.*,2015]. The cobalt complexes with salicylaldehyde and diamine have excellent light resistance and storage properties, and they do not deteriorate in acidic gases like CO_2 [Anis,ltrat.*et.al.*,2013]. Novel tetradentate Schiff bases are utilized as a chromogenic reagent to detect nickel in some natural food samples [Bethanu,Asnake Lealen,*et.al.*,2019]. In the presence of ethylene diamine, photochemical breakdown of natural rubber yields ATNR

(amine terminated liquid natural rubber).ATNR creates poly Schiff bases when it is handled with glyoxal, which increases age resistance.[Kim,Hynwoo,et.al.,2010]. Organocobalt complexes with Tridentate Schiff bases act as a catalyst for the co-polymerization of dienyl and vinyl monomers in emulsions [Pytlakowska,K.,*et.al*.,2013].

1.1.5-Agricultural applications

Schiff bases are used in agriculture as pesticides as well as plant growth regulators. Certain Schiff bases have been found to be poisonous to insects. Sulfanethiodiazole and salicylaldehyde or thiophene-2-aldehyde, as well as their metal complexes, are examples of Schiff bases [K.S.Siddiqi,*et.al.*,1988]. When these Schiff bases are combined with Mo(IV), they have insecticidal effect against ball worms and help mung bean sprouts survive longer [Herrera-Gonzalez,et.al.,2019]. The insecticidal action of a pesticide can be improved by fluorinating the aldehyde component [Armarego,Wilfred,L.F2017]. Schiff bases have also been shown to have a major effect on plant hormones like auxins and cytokinins, as well as root growth [V A.Joseph,*et.al.*,2015]. N-acylated chemicals have been shown to impede the growth of wheat, rye, and barley seedlings [Nair,*et.al.*,2012]. Auxins and cytokins, as well as Schiff bases of thiodiazole, exhibit significant plant growth regulator function [X.Song,*et.al.*,2005].

1.1.6-Application as catalysts

In the oxidation of cyclohexane to cyclohexanol and cyclohexenone in the presence of H_2O_2, Schiff base complexes of Co(II), Fe(III), and Ru(III) produced from hydroxy benzaldehyde are utilized as catalysts [Kirillov,*et.al.*,2012].In the forward scan of Co(III) complexes of indoxyl thiosemi carabazone (ITSC), one pair of well-defined reduction peaks at

various potentials represent the reduction of Co^{+3} to Co^{+2} by one electron process and subsequent oxidation of Co^{+2}. The inherent reducing propensity of the thiosemicarbazone ligand explains the Co^{+3}/ Co^{+2} quasi reversible character [A.Murugkar,*et.al.*,1999]. In the presence of an activator, Ni(II) complexes with Bidentate (N-N) ligands constitute an effective catalyst precursor for olefin oligomerization[Haddad,Zoubida,*et. al*.,2014], because a large range of Co(II) complexes may reversibly bind oxygen, they're widely used as model compounds for natural oxygen carriers. Due to their catalytic capabilities at mild circumstances, they are employed in O_2 storage as well as chemical synthesis [Dey,Suman Kr.,*et.al.*,2016].

1.1.7-Applications in analytical chemistry

Schiff bases have been reported to be used in both qualitative and quantitative investigations. For quantitative determinations of metal ions, a variety of Schiff basechelating agents utilized for metal ion detection can be used. The techniques are mostly the same in most circumstances. The above application's major stage is complexformation, which is primarily influenced by pH, temperature, cation size, and ligand structure. The new analytical method has a good selectivity due to optimization of these parameters to improve the stability of the complexes [Gouda, Aymam,.*et.al.*,2016].

1.1.7.1-Photometric method of analysis

For the detection and quality determination of trace elements, photometric approaches have been widely applied. They are based on the color creation caused by the Schiff bases reacting with the ions,for example, is a brown complex formed by o-[N-(o-hydroxyphenyl) forminidoyl]-phenol with Mn(II) at pH 9.1 to 11.6. For the

spectrophotometric measurement of uranium(VI), 2,2(2,6-pyridiniyl BIS methylidynenitrito) phenol has been utilized [Abd El-Lateef,Hany M.,2015]. The abosorbtivity is 1.9 x 104L $mol^{-1}cm^{-1}$ and the red color generated is measured at 500nm. By extracting Pd(II)-biacetyl monoxime-2-pyridyl hydrazone (BMPH) from an aqueous acidic solution into chloroform and forming a purple reddish complex, the trace level of palladium(II) was detected. Pd(II)BMPH complex has a molar abosorbtivity of around 7500 L $mol^{-1}cm^{-1}$. at 560nm in the chloroform extract [Tarn, Hoang Vinh,*et.al.*,2010].

1.1.7.2-Fluorometryin analysis

Holezbecher reported that Schiff bases obtained from salicylaldehyde and aniline fluoresce in alkaline medium and therefore can be used as indicators for acid base titrations. He proposed o-[-(o-hydroxyphenyl)formidoyl]phenol for quantitative determination of Aluminum. The analytical importance of such indicators lies in the fact that they make possible acid-base titration in color red solutions when the use of conventional indicators is precluded. In this analysis there is always the dependence of fluorescence on the pH similar to that of acid-base fluorescence indicators. It is a good method for the detection and determination of inorganic ions [G Prajapti,*et.al*.,2021].

1.1.7.3-Potentiometric sensors

A bromide sensor based on Fe(III)-salen was also developed. This sensor exhibits a strong bromide selectivity for a variety of organic and inorganic anions, including iodide, chloride, and hydroxide ions [Aragay,*et.al*.,2011]. Salen is a tetradentate –O-N-N-O- donor Schiff base made from two equivalences of salicylic aldehyde and a diamine. It takes the shape of square planer metal complexes. As cation carriers in

potentiometric sensors, a variety of Schiff base ligands have been used because they provide exceptional selectivity, sensitivity, and stability for certain metal ions. The advantage of this type of analysis is that it is inexpensive, highly sensitive, and highly selective. Ionic activity detection [Mohan,Anandhu,*et.al*.,2021].

1.1.7.4-Schiff base as solvent exractant

The influence of ligand atoms on the liquid-liquid extraction of bi-valent transition metals was investigated using macrocyclic Schiff bases comprising thiophene or phenol subunits. The phenol groups in the macrocycle cause a boost in transition metal ion extraction. Acyclic Schiff bases were also discovered to have a higher extractability than macrocyclic Schiff bases [Falcaro, Paolo,*et.al.*,2016].

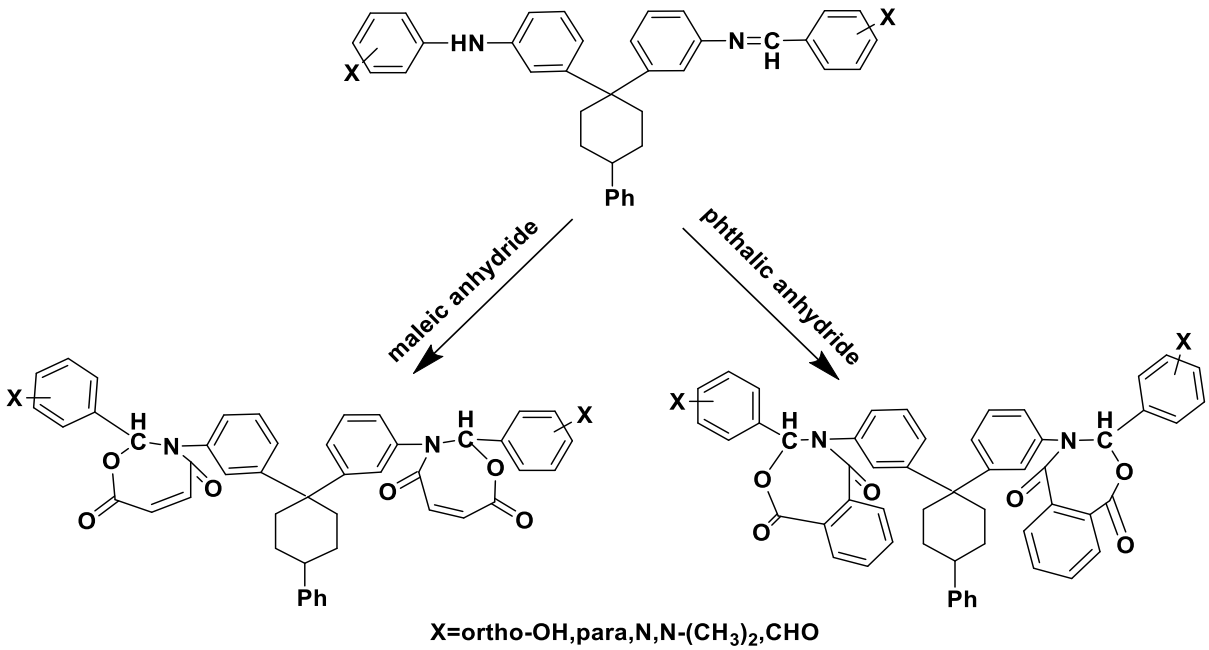
1.1.7.5-Application in HPLC

Schiff base metal chelates are metal chelates that can be extracted. On a column of 10 m diameter silica, neutral Ni and Cu chelates of two representative Schiff base ligands, N-N-ethylene bis (acetyl acetone imine) and N-N-ethylene bis (salicylald-imine), were separated. When the mobile phase is4:1 methylene chloride: acentonitrile, both pairs of chelates are successfully resolved with high peak shape efficiency [Mcknight, Ursula S.,*et.al*.,2015].

1.1.8-Schiff bases are used as methods of preparation:-

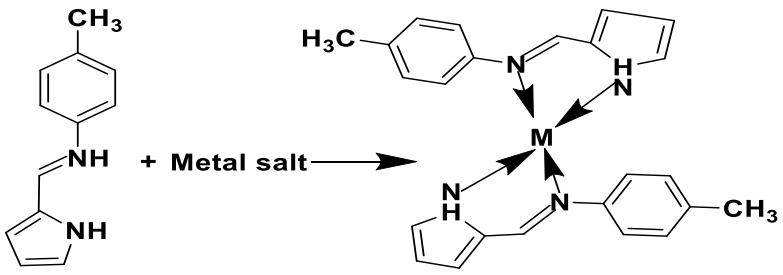
One of the important applications of Schiff bases is the preparation of many organic compounds and complexes:-

1- [Nief, Olfat ,*et.al*.,2011] Scheme (1)



Scheme 1.1:Structures formal of the new prepared compounds.

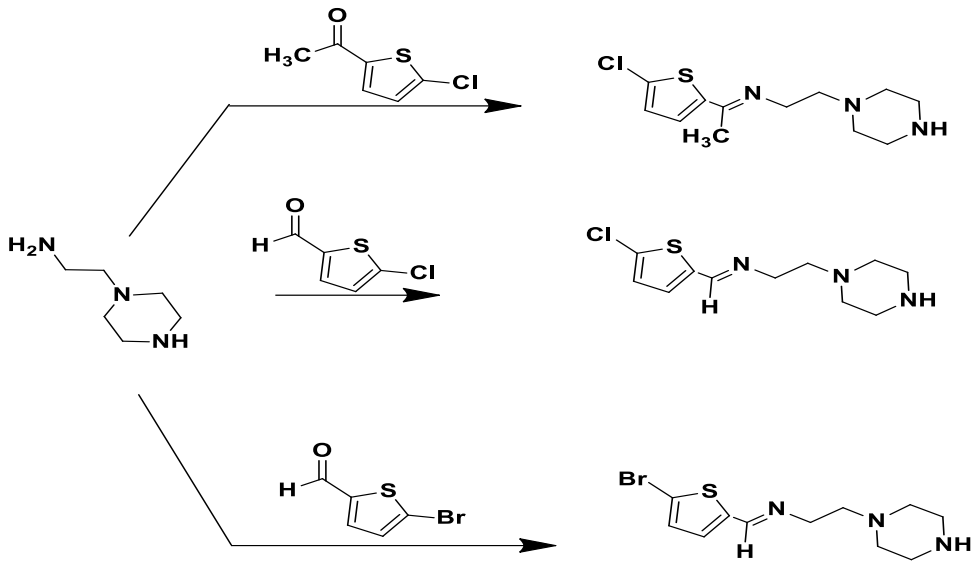
2-[Charles ,A.*et.al.*,2019] Scheme (2)



Scheme 1.2: Synthesis of metal complexes from Schiff base

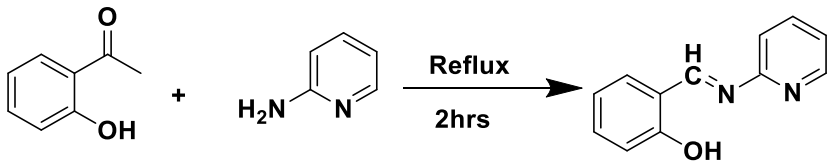
1.2-Synthesis of Schiff Base Compounds:

[warad,Ismail,*et.al.*,2020]Have use,1-(5-chlorothiophen-2-yl) thenone thiophene-2-carbaldehyde,and 5-bromothiophene-2carbaldehyde, which afforded the good yields formation of N-(1-(5-chlorothiophen-2-yl)ethylidene)-2-(piperazin-1-yl)ethanamine(L1),2-(piperazin-1-yl)-N-(thiophen-2-ylmethylene)-ethanamine (L2), and N-((5-bromothiophen-2-yl)methylene)-2-(piperazin-1-yl)ethanamine(L3), respectively (Scheme3).



Scheme 1.3:Synthesis of the Schiff bases L1 –L3.

[Chundawte,*et.al*.,2014]Have use 2-amino pyridine and salicyladehyde to give N-(2-hydroxylben zylidene)Pyridine-2-amine.



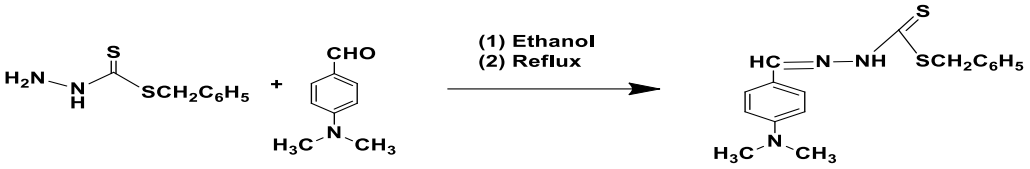
Eq.1.1: Preparation of N-(2-hydroxylben zylidene) Pyridine-2-amine

[Kudrat-E-Zahan,*et.al.*,2015] Have use benzyl N'-(4-dimethylamino-benzylidene)hydrazinecarbodithioate (SB), was synthesized in high yield by the condensation of S-benzyldithiocarbazate(SBDTC)with 4-(dimethyl -amino)benzaldehyde in a neutral medium.

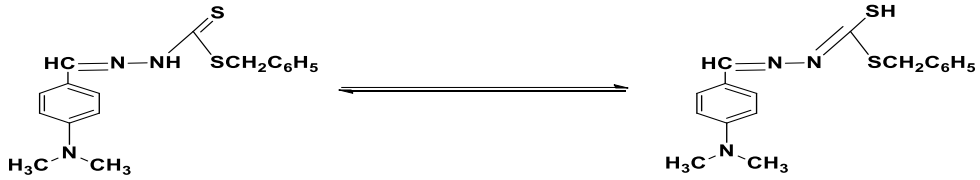
The Ni(II), Cu(II), and Zn(II) complexes were obtained by reacting the synthesized Schiff base with the corresponding metal nitrates:

$M(NO3)_2 \cdot nH2O + SB \rightarrow [\ M(II)(SB)_2]$,

Where M(II)=Ni(II), Cu(II), Zn(II) and SB=benzylN'-(4 imethylamino-benzylidene)hydrazinecarbodithioate.As known, hydrazinecarbodithioic acid exists in solutions as a mixture of the thione and thiol tautomers.

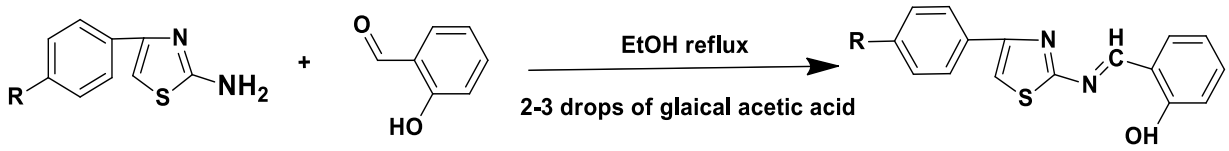


Eq.1.2



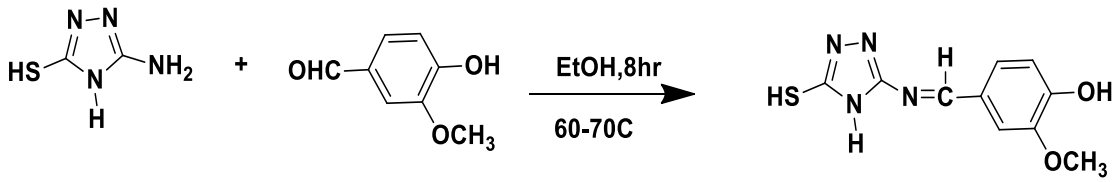
Eq.1.3

[Aldelfy,*et.al*.,2019] A mixture of 2-amine -4(4-substituted phenyl) thiazole in absolute ethanol and salicylaldehyde and catalytical amount of glacial acetic acid the synthesis of the Schiff base ligands 2-Hydroxybenzylidene-4-phenyl - 2-amino thiazole:-



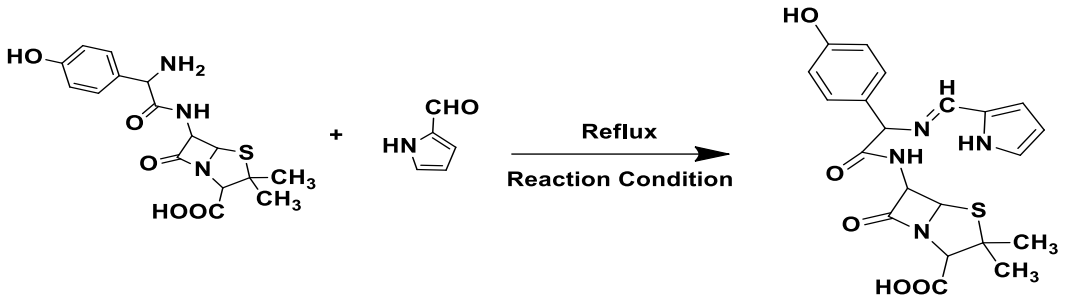
Eq.1.4: R:H(L1) , NO_2(L_2) , CH_3(L_2) , OCH_3(L_3) , F(L_5) , Cl(L_6)

[Vinush,H.M.,*et.al.*,2019] An equimolar mixture of an ethanolic solution of 5-amino-4H-1,2,4- triazole-3-thiol and 3-hydroxy-4-methoxybenzaldehyde the synthesis of Schiff base ligands:-



Eq.1.5

[Mouayed Y.Kadhum,*et.al.*,2014]Using the Primary amine compound to interact with the carbonyl compound to give the final compound azomethine.



Eq.1.6

The Schiff base, which was synthesized from amoxicillin and salicylaldehyde and identified as a bidentate ligand, was employed. Bacterial experiments were conducted on three species, with the results indicating in- Metal complexes' antimicrobial activity is improving. See the diagram below[Reiss, A., *et. al*.,(2015)].

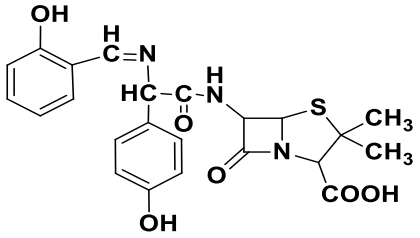


Figure 1.10: Structure of Schiff base from amoxicillin and salicylaldehyde

1.3-Historical perspective:

Antimicrobials are defined as any agent that has inhibitory or lethal actions against microorganisms. Antibiotic is a more limited phrase that denotes the use of antibiotics. The antibacterial agent comes from a natural source. Similarly, under-researched ،The term "chemotherapeutic" was coined by accident. A chemically synthesized antibacterial agent [Verma,Kanika,*et.al.*,2021]. Initially, Antibiotics were once thought to

have a low molecular weight. Organic compounds or metabolites that are produced as a result of certain microorganisms vs. others living in the same environment 'habitat,' and they're fighting for the same nutrients. However, Some authors, most notably Davies [Spoangnolo,*et.al.*,2021], have recently been criticized. Attempting to start a conversation by implying that in the environment the vast majority of these chemicals are vital. In natural settings, they play a role in the control of metabolic function. Colonies of microbes, if this idea is correct, Antibiotics are crucial chemical messengers that serve as signaling molecules between cells in a microbial ecosystem molecules[Sharma,Girraj,*et.al.*,2021]. In 1928, Alexander Fleming discovered penicillin's antimicrobial properties. Fleming saw something interesting while working on another bacteriological problem. A Staphylococcus aureus culture infected with Penicillium notate is a type of mold. Fleming was a remarkable observer. He's a dis- he kept working on the project he was working on capable of describing the substance that surrounds the mold It then isolates it. He gave it the name penicillin and published it.his findings, as well as several penicillin uses [Azman ,Adzzie-Shazleen ,*et.al*.,2015].

The first one, however, did not appear until 1940. A penicillin clinical trial was conducted against an Infection with streptococci in a mouse model. The first β-lactam antibiotic was found in this year. In fact, the chemical structure of penicillin was discovered. Later, by Hodgkin et al. [Martin Garcia,.2021], by the use of X-ray crystallography was used. One of the images used by Sir Alexander Fleming Nobel in the Award lecturer is Fig.(1.11).in 1945, and depicts a S. aureus-free circle around the P. notatum is a species of plant that grows in the United States (mold).

The reactive β-lactam ring system, a highly strained and reactive cyclic amide, is present in all of the currently known b-lactam antibiotics. There are five significant factors to consider. penam, penem, carbapenem, and other ring systems ring structure of Penicillin's are part of a wide category of β-lactams known as penams.

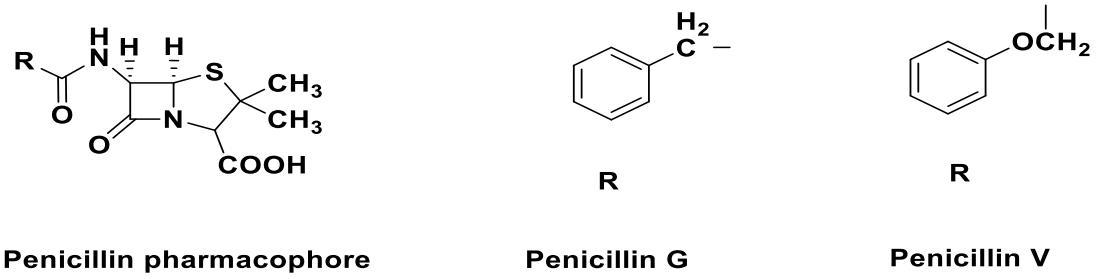


Figure 1.11:Penicillin pharmacophore and penicillin G and Penicillin V

As a result, penicillin's have a bicyclic structure called 6-aminopenicillanic acid, or 6-APA. This The structure is made up of a dipeptide that has been encapsulated. L-cystein and D-valine combine to become L-cystein and D-valine. in the thiazolidinic ring and in the b-lactam ring [Arzanlou.,*et.al*.,2017]. The β-lactam ring system's reactive nature makes Penicillin's (penams) and similar chemicals are prone to contamination. A wide range of derivative processes The β-lactam ring is reconfigured in acidic conditions and at room temperature, starting with the protonation of the β-lactam nitrogen and ending with the protonation of the β-lactam nitrogen. The remaining lateral chain's nucleophilic assault carbonyl. The oxazolin intermediate ring will be formed.penillic acid by forming a new imidazole [Arzanlou.,*et.al*.,2017]. This Due to stomach acidity, this procedure has some clinical importance. As a result, in order to administer orally, these Compounds must be protected from acidic environments. Finally, high-acid situations necessitate therapies. Thiazolidini and penicillin-derived β-lactam ring Among other things, I have my. It's a chelating agent, thus it's good for you. Penicillinamine can

also be utilized after exposure to heavy metals. Heavy metal poisoning in rheumatoid arthritis arthritis, and other inflammatory diseases [American.,*et.al.*,2010]. Penicillin's G and V, for example, were originally made by fermentation and were often combinations of other β-lactams (Fig.1.11). 6-APA is now available. Hundreds of synthetic and biological organisms have been created as a result of this breakthrough. Penicillins that are semi-synthetic. Many bacteria produce a collection of enzymes that are specially intended to degrade and inactivate β-lactams, in addition to chemical degradation. These enzymes play an important role in the body. Penicillinases are a group of enzymes that work together to break down penicillin. By far the most popular The β-lactamase is the most common kind of penicillinase. It targets and breaks the β-lactam binding directly Antibiotic inactivation [Dellinger,R.Phillip,*et.al*.,2013]. There are also a number of options acetyl transverses dentified from bacteria These enzymes break the antibiotic's acylamino side-chain, rendering the antibiotic inactive molecule. Methicillin was the first molecule to be synthesized, and it varies from benzyl penicillin in that it has methoxy substitutions at positions 2' and 6' of the benzene ring. Groups, resulting in steric hindrance in the vicinity of the amide bound[Wang,Chunling,*et.al.*,2021].

Nafcillin,and ancillin are other molecules that have been produced and are similar to methicilin in terms of steric hindrance. These are the molecules that This penicillin belongs to the first category of manufactured penicillins. However, these changes result in a general decline in the efficacy of β-lactams, as well as Almost all β-lactamase-resistant penicillin's on the market are less effective than the parent molecules. Some chemicals, such as clavulanic acid, tazobactam, and

sulbactams, are now available that can bind to β-lactamases irreversibly and thereby inactivate them. There are pharmacological formulations that produce certain outcomes. The result of combining penicillin's with b-lactamase[Zaffiri, Lorenzo ،*et.al*,2012]. Resistance to β-lactams mechanisms Ampicillin and amoxicillin are penicillinase-sensitive, orally active antibiotics that have a phenyl glycine moiety in place of the phenyl acetic acid moiety. These antibiotics have a wide range of uses. They have a broader spectrum than penicillin G, but they are not as effective. β-lactamase susceptible They're frequently accompanied with To avoid enzymatic breakdown, clavulanic acid is used. Another effect of b-lactam reactivity is the In vivo production of allergic haptens Nucleophilic On some substances, hydroxyl (OH) or sulphydryl (SH) groups are present. Proteins can react with the b-lactam ring system, forming a covalent penicillin–protein compound that can cause an allergic reaction, explaining the inherent allergy risk. [Johansen,Jeanne D.,*et.al.*,2015].

1.3.1. 6-Aminopenicillanic Acid:-

6-Aminopenicellanic acid (6-APA), a key intermediary in the manufacture of semisynthetic antibiotics, is essentially the original antibiotic's nucleus. The molecule of penicillin. For a long time, enzyme transformations have been utilized to synthesize pharmaceutical compounds of diverse kinds [Aharnowetz and Choen, 1992] [Solano,D.Munoz,*et.al*.,2012]. The majority of microbial changes have been [Sambyal,*et.al.*,2021; Walsh,Gary,*et.al.*,2014] ploited in the field of steroids and antibiotics. Penicillin's are the most extensively used β-lactam antibiotics, accounting for roughly 19% of all prescriptions.

Due to their stronger inhibitory activity on bacterial cells, they have dominated the global antibiotic market. Wall synthesis, antibacterial action across a broad spectrum, minimal toxicity, and high efficacy against a wide range of bacterial strains However, overuse of these antibiotics has resulted in bacterial resistance.[Hamed,Imen.,2016] .

The antibacterial activity of the produced compounds was investigated using the interaction of 6-amino penicillanic acid (6- APA) with Salicyldehyde , Benzyldehyde , and O-Nitrobenzyldehyde. Staphylococcus aureus, Streptococcus faecalis, Proteus mirabilis, and Pseudomonas aeruginosa)The antibacterial activity of the produced ligands compounds is higher, as shown in the diagram below[B. Q . Ali *et.al*.,(2016)].

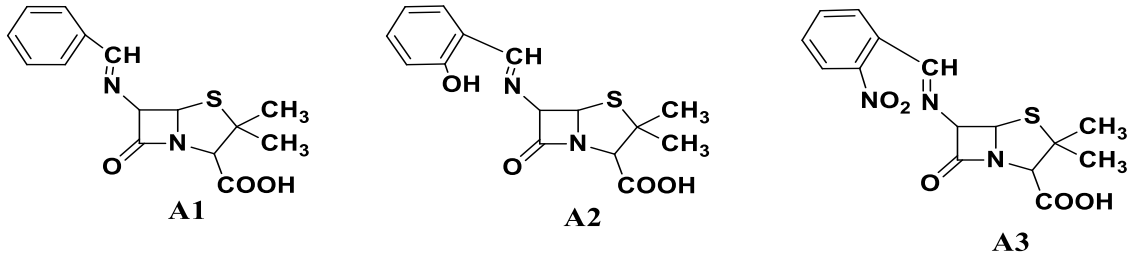


Figure 1.12: Structure of A1,A2,A3

1.3.2-Enzymatic modification of penicillins to 6-aminopenicillanic acid (6-APA)

Penicillin acylases or amidases are used in soluble or immobilized form under acidic or alkaline conditions for the enzymatic conversion of penicillins to 6-APA and semisynthetic penicillins .Classification of penicillin acylases to 6-aminopenicillanic acid (6-APA)Penicillin acylase was first isolated from Penicillium chrysogenum Q176 [Parmar, Anupama, *et.al*., 2000]Many microbial sources for the enzyme are now known and have been extensively .

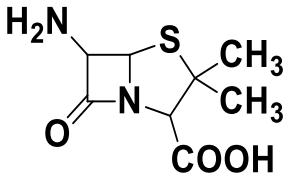
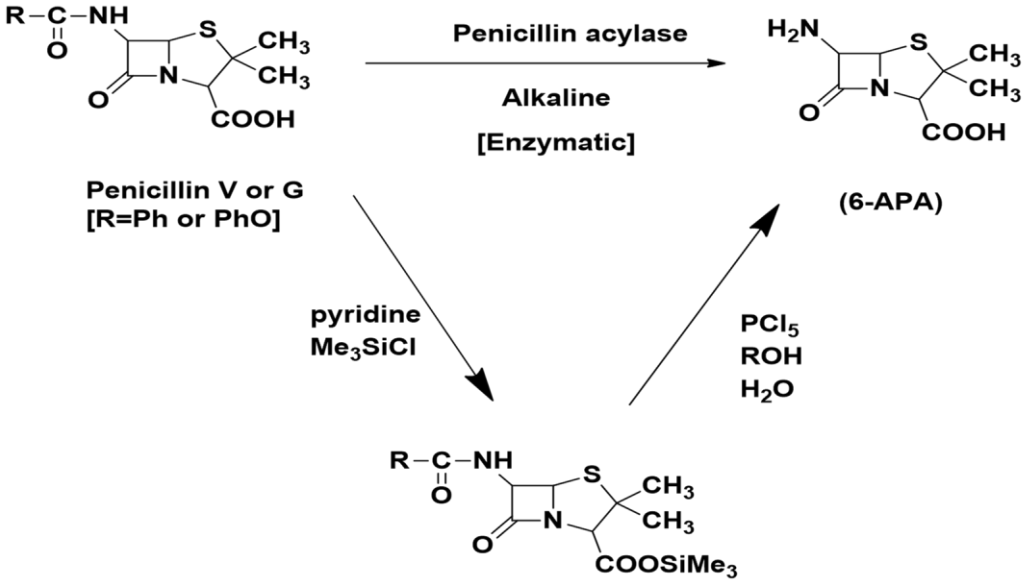
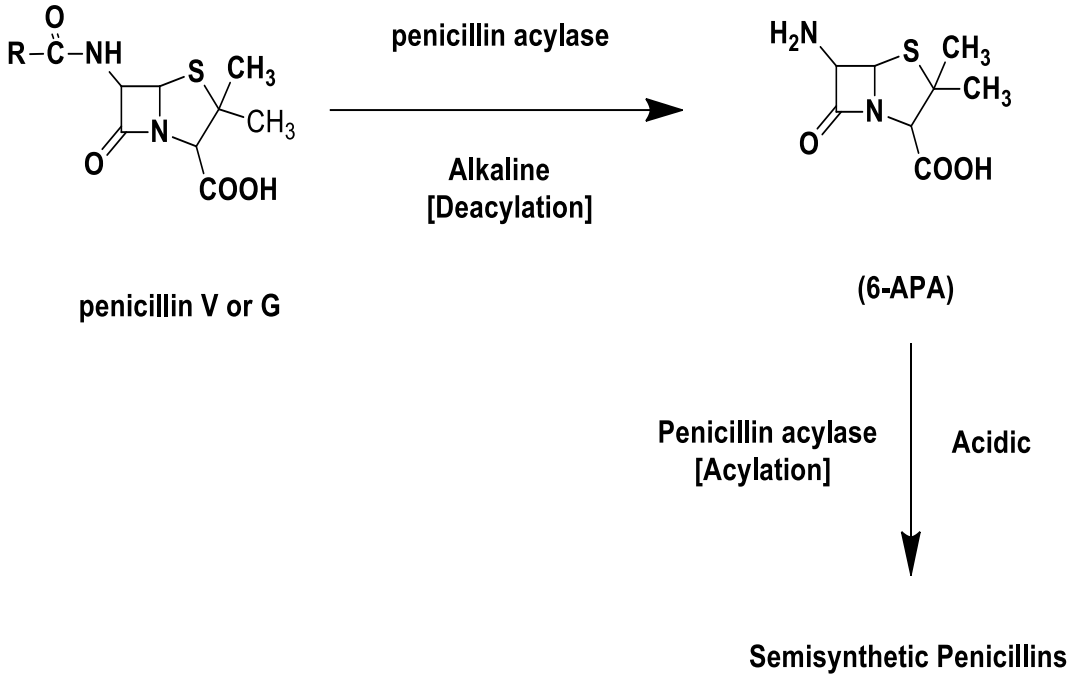


Figure 1.13:Chemical structure of 6-APA



Scheme 1.4: Chemical and enzymatic deacylation of penicillins to 6-APA.

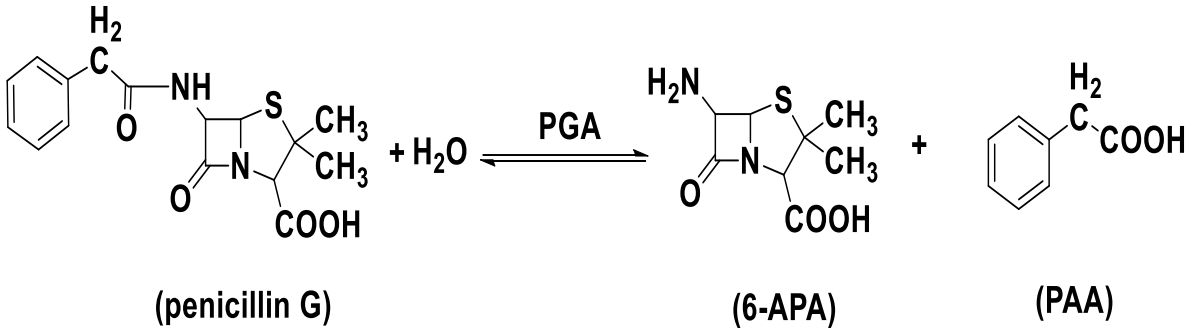


Scheme 1.5:Enzymatic modification of penicillins to 6-APA and semisynthetic penicillins

Most medications have electron donor groups that can bind naturally occurring metal ions, including 6-aminopenicillanic acid (APA) [M.J. Bojczuk,1993]. In blood plasma, essential trace metal ions like zinc and copper are present in far too low amounts to have a substantial impact on these medicines' bioavailability Antibiotics are believed to be effective. The capacity of these chemicals to form complexes with metals is connected to their activity.Antibiotics as ligands have been studied for their complexion capabilities thanks to ions.It is generally known that multimetal–multiligand equilibria play a role in biological systems well-known.[M.M. Shoukry,1995]

Penicillin G acylase (PGA) works by intermediating antibiotics by acting on the side chains of penicillin G, cephalosporin G, and other similar antibiotics,6-amino penicillanic acid (6-APA) , leaving behind phenyl

acetic acid (PAA) as a common by-product (Scheme1.6) . [Arroyo M, *et.al.*,2003, Rajendhran J, et.al,2003]

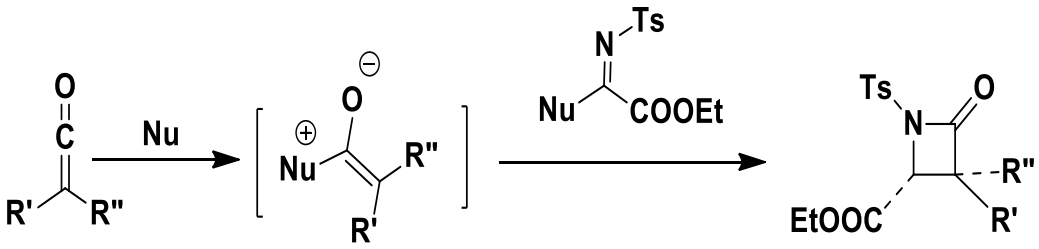


Scheme 1.6:(6-APA and PAA)

1.4.β-Lactam

β-lactam is a four-membered ring saturated heterocyclic molecule with one nitrogen atom and one carbonyl group [I k Jassm *et.al.*,2011]. Its heterocyclic non-aromatic compound [T Eicher., 2003]. It belongs to the Azetidine ring class [NAA El-Kanzi,*et.al.*,2012].The most important use of -lactam is in the manufacture of penicillin [AD Deshpande *et.al.*,2004], where it serves as the penicillin's function group. As a result, it binds to the active site of the Transpeptidase enzyme, which is a bacterial enzyme that cross-links amino acids.To build stiff cell walls, peptidoglycan chains are used [Nathan,Arokia,*et.al*,2021,Gordon,E,2000].

Only one catalytic, asymmetric synthesis of the β-lactam ring system is known,affordingproductInmodest,enantioselectivity[Takeda,Youhei,*et.al.* ,2016]Many asymmetric auxiliary-based β-lactam syntheses rely on the reaction of imines with ketenes, a process that generally proceeds without a catalyst[Tan, Ningzhi,2017] .We recently accomplished a catalyzed reaction of imines and ketenes by making the imine component non-nucleophilic[Guo,Xin,2013]



Scheme 1.7 : β-lactam syntheses

1.5-Heterocyclic compounds.

The aromatic heterocyclic side groups of the most prevalent and important constituents of living cells, heterocyclic play a crucial part in biological processes [A. S. Anees *at el*, 2011]. Heterocyclic molecules are well known to play a critical role in health care and pharmaceutical drug design. Currently a number of heterocyclic compounds are available commercially as antibacterial drugs and great efforts have been put to the identification of novel antibacterial targets for novel antibacterial drug discovery[Dholakia S.P *at.el* 2011]. Schiff bases can be derived from o-aminophenol. These are the compounds containing characteristic -C=N- group. The development and synthesis of novel Schiff bases derivatives as potential chemotherapeutics still attracts the attention of organic and

medicinal chemist. Besides their potential use as biologically active agents[S.Sharma *at el* 2012]. Nitrogen-containing heterocyclic possess diverse chemotherapeutic activities[Wasfy A.F *at.el.*,2013]. Various compounds such as alkaloids, essential amino acids, vitamins, hemoglobin, hormones, large number of synthetic drugs and dyes contain heterocyclic ring systems. There are a large number of synthetic heterocyclic compounds, like pyrrole, pyrrolidine, furan, thiophene, piperidine, pyridineand and thiazole having important application and many are important intermediates in synthesis[Singh R at el 2014]**.** Organic heterocyclic compounds are formed when a non-carbon atom is incorporated into an organic cyclic structure [G.Editorial 2005]. "Heterocyclic Chemistry" is a branch of chemistry concerned with the synthesis, characteristics, and uses of heterocyclic structures. Since the 1800s, heterocyclic chemistry has been researched as a field of organic chemistry [K.T. Nakhate *at el* 2017]. The prefix hetero denotes the incorporation of at least one non-carbon element, such as oxygen, nitrogen, or sulfur, into an aromatic or partially or fully saturated cyclic system [A.V. Rane 2016]. The five- and six-membered rings that contain one heteroatom, such as furan 1, pyrrole 2, thiophene 3, pyridine 4 and peperidine 5, are the most prevalent heterocyclic structures, as shown in Figure 1.14

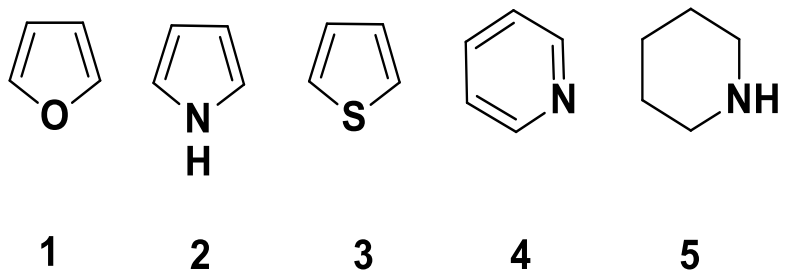


Figure 1.14: Common five- and six-membered ring with one heteroatom.

In addition, these five- and six-membered heterocyclic structures may contain two heteroatoms to produce heterocyclic structure such as pyrzole **6**, oxazole **7**, thiazole **8**, pyrmidine **9** and pyrazine **10** as shown in Figure (1.15) [P.Ramanathan 2018].

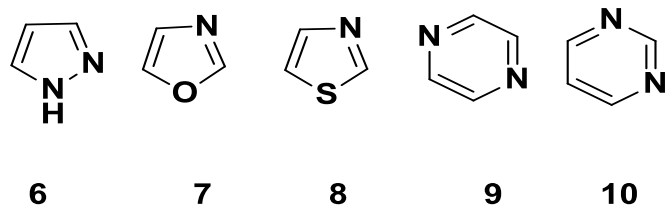


Figure1.15: Common five and six-membered ring with two heteroatoms

Moreover, if these five- and six-membered ring systems are fused with benzene ring, it leads to generate a new aromatic heterocyclic ring system with different structures such as quinolone **11**, indole **12**, benzo furan **13** and benzothiophene **14** as shown in Figure (1.16) [R.Dua *at.el.*, 2011].

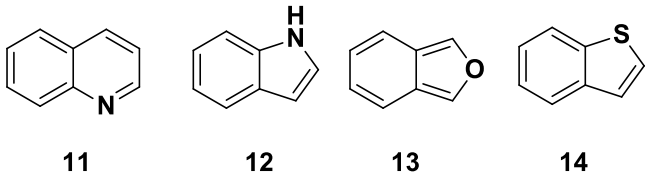


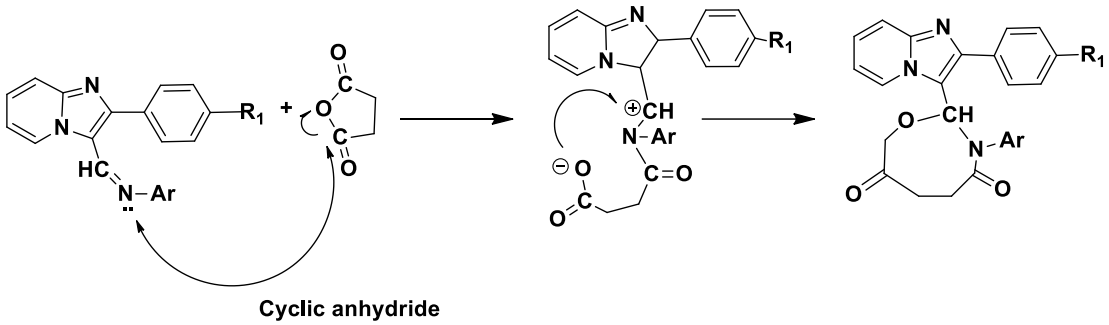
Figure 1.16: Common benzo fused aromatic heterocyclic structures

In general, heterocyclic compounds are making up more than half of all known organic compounds [Y. Özkay.H.K .Gencer *at.el.*, 2015]. Most of these heterocyclic compounds are presented in a wide variety of most vitamins [J. R. Anacona at el 2013], many natural products [S.A.S 2015], biomolecules such as nucleic acids [A. A. Fadda *at.el.*,2014], and biologically active compounds that act as drugs used as anticonvulsants [A. H. K. Sharba at el 2011], antiseptics [J. O. Otutu 2013] and antihistaminics [A. Al-mulla 2017]. Moreover, heterocyclic compounds have different applications in diverse fields such as agriculture [J. Patil 2016], polymer [M. Hossain at el 2018] and various industries [M.Vinicius *at.el.*, 2005]. Among

different compounds containing heterocyclic compounds, antipyrine compound plays an important role in the modern organic synthesis, not only because it constitutes a particularly useful class of heterocyclic compounds but also because it is of a great biological interest [C.Hadole *at.el.*, 2018].

1.6-Oxazepines:-

Oxazepine–dione is a seven-membered ring with nitrogen, oxygen, and two carbonyl groups. Psychoactive drug [Basavaraju *at.el.*, 2007], enzyme inhibitors, and other biological pharmacological actions of oxyazepine and its derivatives [Zainab Amer S. *at.el.*, 2011and Patent Evaluation 1992]. as well as analgesic [Martin Kratzel 1994]. Diazepine-dione is a seven-membered ring with two nitrogen atoms in it atoms at positions 1,2, 1.3, and 1.4, as well as two carbonyl groups [G.W.H Chesman *at.el.*,1979], diazepine-dione. Anti-cancer [Min Xie at.el.,2016] and hepatitis [Peng Zhang,*at.el*.,2005]. The CNS activity of 1,3-oxazepine was discovered, and it's now utilized to treat anxiety and stress, as well as muscle spasms[Y.Deng,*at.el.*,2016].The mechanism synthesis of oxazepine shown under(Al-Lami and Salom,) Scheme(1.8)



Scheme 1.8 mechanism synthesis of oxazepine

1.6.1-Oxazepines Ring system:-

Oxazepine ring system is an unsaturated seven-membered heterocyclic ring having two heteroatoms (O and N) was reported in 1965

[R. M. Al-juburi 2012]. Depending on the position of the nitrogen atom related to the oxygen atom, there are three isomeric structures of oxazepine ring system; 1,2-oxazepine **15,** 1,3-oxazepine **16** and 1,4-oxazepine **17** as shown in Figure 1.15 [J.Al and A.Hasan 2016].

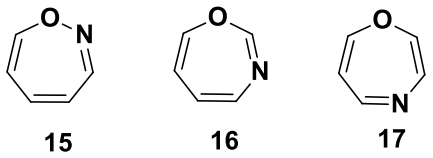


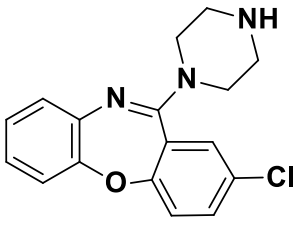
Figure 1.17: **Isomeric structures of oxazepine ring system**

According to Hückel's rule, oxazepine ring system is not aromatic system and it is also not-planar, thus takes the shape of boat to increase its stability system [H.Kf and E.Hh 2013]. During the last decades, 1,3-oxazepine ring system was gained much attention in pharmaceutical industry and medicinal chemistry due to the fact that this structure is present in a large number of compounds with a broad range of different biological activities [S.Thaer ,*at.el.*,2016].

1.6.2-Biological Activities of ox azapine's and Importrance:-

Bacterial resistance to most antibiotics is on the rise, posing a serious threat to health care [Linden, 2002; Medino *et al*., 2000; Spera and Farber, 2000 ,1994], and new treatments are urgently required. The focus of the search has been on the development of novel antibacterial agents that have new targets Compounds having N,O in modest and large amounts Rings are notable synthetic targets since they come in a variety of shapes and sizes have a diverse set of biological functions [Seto, 2004;Seto and Asano, 2007; Mishra and Panda, 2007; As-Soumatine *et al*., 2004)] .The oxazepines and their fused derivatives [McGee *et.al.*, 2005] have a wide range of biological activities [McGee *et.al.*, 2005]

.Biological processes, Molecules having the oxazepine nucleus have biological, medical, and pharmacological implications[Tripathi el at 1984]such as enzyme inhibitors[Levinspial O,.*et.al.*,1995]. Analgesic [Aiello F.,et al 2004] is a term used to describe a substance that relieves pain. Antidepressants[Pecher J.*et.al.*,1978] and psychoactive drugs [Halina K. ,*et.al.*,2012] are examples of these types of substances. Nucleus of the oxyazepine is a drug that is used to treat depression, anxiety, and agitation [Ayab H, *et.al.*, 2002]**.** 1,3-oxazipene derivatives are also available. These compounds, which are made by reacting Schiff's bases with maleic anhydrid, have been discovered to have biological activities such as antibacterial, antifungal, and anticancer [Aralmarugan S.k. *et.al.*, 2010 and Wadeher J.S,.*et al* 2009].Oxazepine and their derivatives have some important biological pharmacological activities [J.Mikim *et.al.*, 2002] such as enzyme inhibitors [D.Gauthier *et. al.*,1999], analgesic [S.Bilgic et al 2009], antidepressant [J.Jiu et al 1977] and psychoactive drug [O.levy *et.al.*,2001]. Amoxapine is a group of drugs called tricyclic antidepressants. It is used to treat symptoms of depression, anxiety and agitation [G.P.Singh 2009] Figure (1.18)



Amoxapine(asendin)

Figure 1.18

Dibenz [b,f]-1,4-oxazepine Figure (1.19) is used in chemical weapons as tear gas. Tear gas is the common name for a low concentration substance, cause pain in eyes, flow of tears and difficulty in keeping eyes open. It is

used mainly in military exercises and in riot control [H.Fakhraian *et.al.*, 2009]

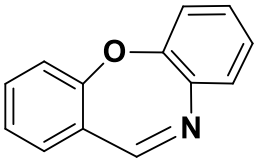


Figure 1.19

prepared new1,3- oxazepine- 4,7- dione derivatives Figure(1.20) [G.Y .Yeap *et.al*., 2010]. and study their liquid crystalline properties.

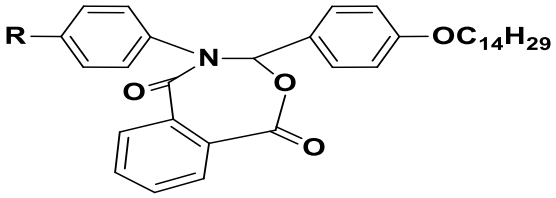


Figure 1.20

[F.Aiello,*et.al*.,2004] prepared 2-Chloro-11(4-methyl-piperazin-1-yl)dibenzo[b,f] [1,4]oxazepine Figure(1.21) and used it as anti-psychoactive.

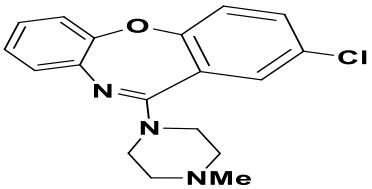
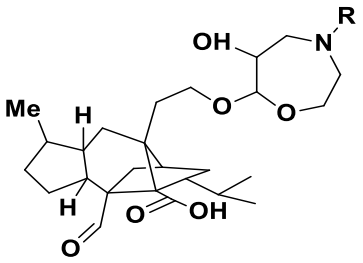


Figure 1.21

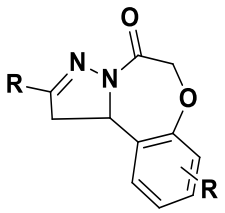
[M.H Serrano-wa, *et.al.*,2002] evaluated the biological activity of 1,4-oxazepine derivative Figure (1.22), medically- known as Sordarin which showed antifungal activity against three types of fungi are candida albicans , candida glabrata and cryptococcus neoformas.



R=-2OME , -Et

Figure 1.22

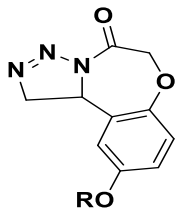
[X.G .Liu *et.al.*,2013] synthesized eight novel 4,5-tetrahydropyrazolo [1,5-d][1,4] oxazepine derivatives Figure (1.23) to be screened for anticancer activity.



R=7,9-2Br,7-Cl,9-OMe,7-CF3,8-NO2,8-Me,9-F,-H

Figure 1.23

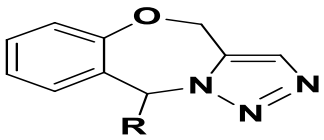
[X.G .Deng,*et.al.*,2010]synthesized novel series of 10-alkoxy-5, 6-dihydro-triazolo[4,3-d] benzo[f][1,4] oxazepine derivatives Figure (1.24) were screened for their anticonvulsant activities by the maximal electroshock (MES) test.



R=-C_2H_5,C_3H_7,n-C_4H_9,C_5H_{11},-$CH_2C_6H_5$

Figure 1.24

synthesized a series of [1,2,3-triazolo [5,1-c][1,4][M.K. seennaiah *et.al.*, 2011]. benzoxazepine derivatives as antibacterial,Figure (1.25)



R=H,aryl,alkyl

Figure 1.25

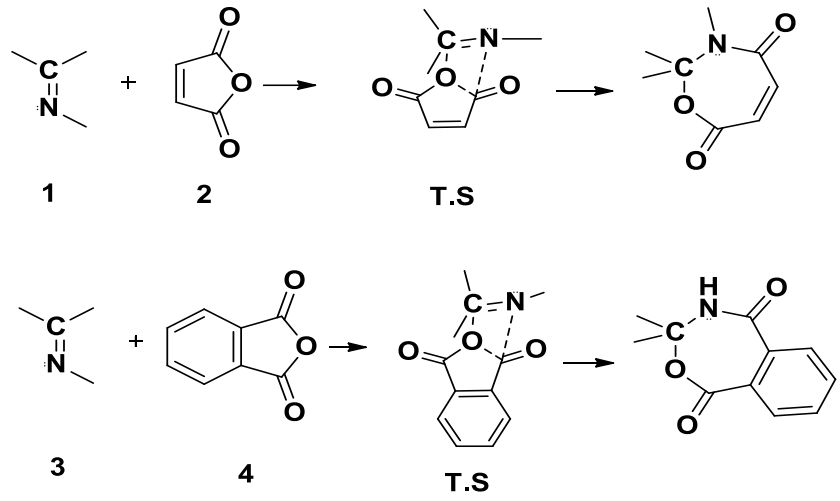
1.6.2.1-Biological Importance of 1,3-Oxazepine Derivatives :-

There is a large number of literatures describing 1,3-oxazepine derivatives for various biological activities such as anticancer [K. M. Mohammad et al 2018], antithrob [Z.G.Alrecabi,*et.al*.,2017], anticonvulsant [S.S. Jasim 2018], antirombotic [Z.Amer 2018], anti-inflammatory [I.K.Naeem *et.al*.,2017], antipsychotic [S.Adnan et al 2014], antidepressant [H.Kf.,and E.Hf 2013], antiviral [Manju ,P et al 2014], and telomerase inhibitors [M.A. Mohammed -Ali *et.al.*, 2014]. Furthermore, 1,3-oxazepine derivatives have a biological activity against different types of bacteria, in addition of their uses as inhibitors of some enzymes action [A. H. Samir *et.al.*, 2017]. Thus, due to this importance in pharmaceutical utilities, the synthesis of new 1,3-oxazepine derivatives is a considerable interests for us[A. M. Asiri *et.al.*, 2010].

1.6.3-Synthesis of oxazapine's:-

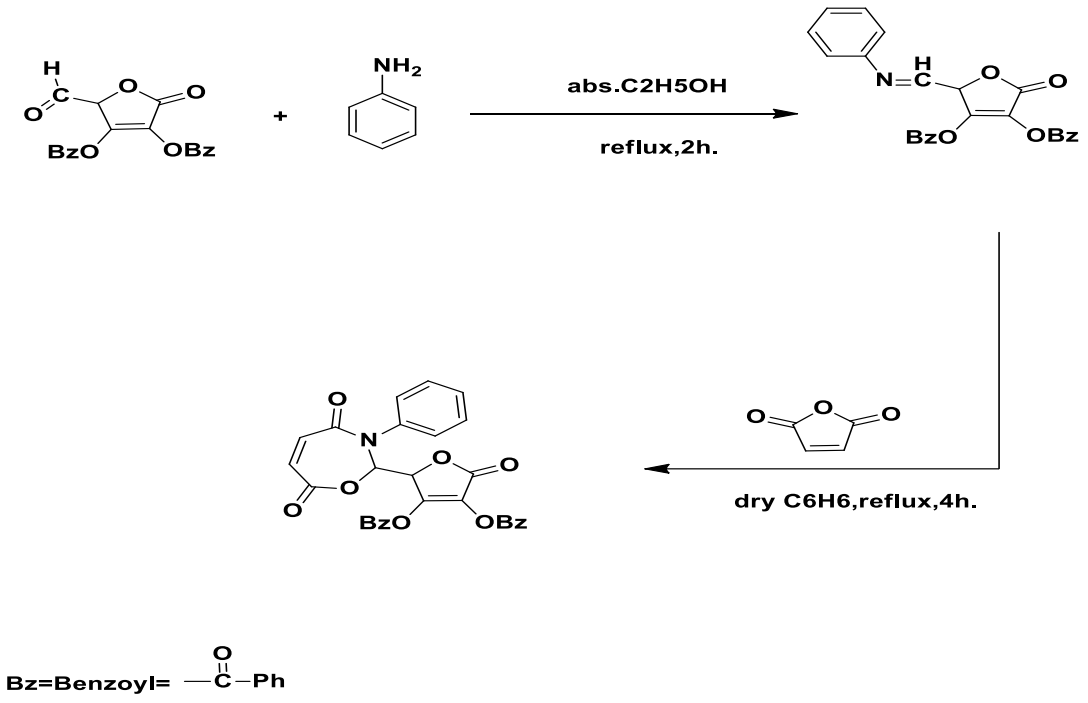
Recently, the common synthetic way that has been used for the synthesis of oxazepine ring system specially 1,3-oxazepine structure is cycloaddition reaction. This reaction is performed by the reaction of imine compounds (Schiff bases) such as compound (**1)** with five atoms

cyclic anhydride such as **(2)** or (**4)** [O. H. Abid *et.al.*,2017] as shown in Scheme **1.9**.



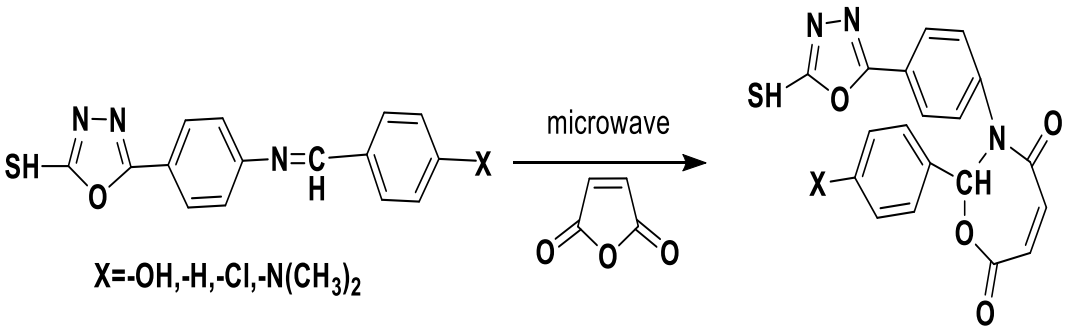
Scheme 1.9: Mechanism of the pericyclic reaction for the synthesis 1,3-oxazepine ring.

[R. S. Jwad *et.al.*,2006] prepared new 1,3-oxazepine derivative starting from. L-Ascorbic acid .Scheme (1-10)



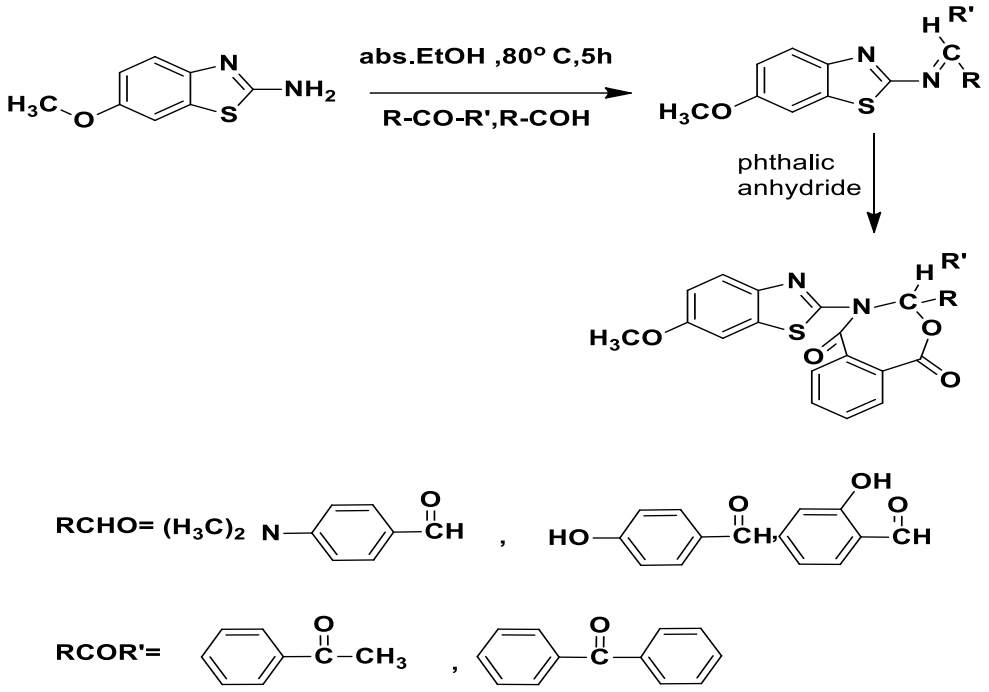
Scheme (1-10): Formation of 1,3-oxazepine derivatives through cycloaddition reaction of imino ascorbic acid to maleic anhydride

[A. Hameed 2012] synthesis of four new 1,3,4-oxadiazole derivatives containing 1,3-oxazepine moiety by microwave assisted organic synthesis method through the addition reaction of 2-[4-(arylidene) phenyl- 1,3,4-oxadiazole-5-thiol] with maleic anhydride under variable.microwave power watt. Scheme (1-11)



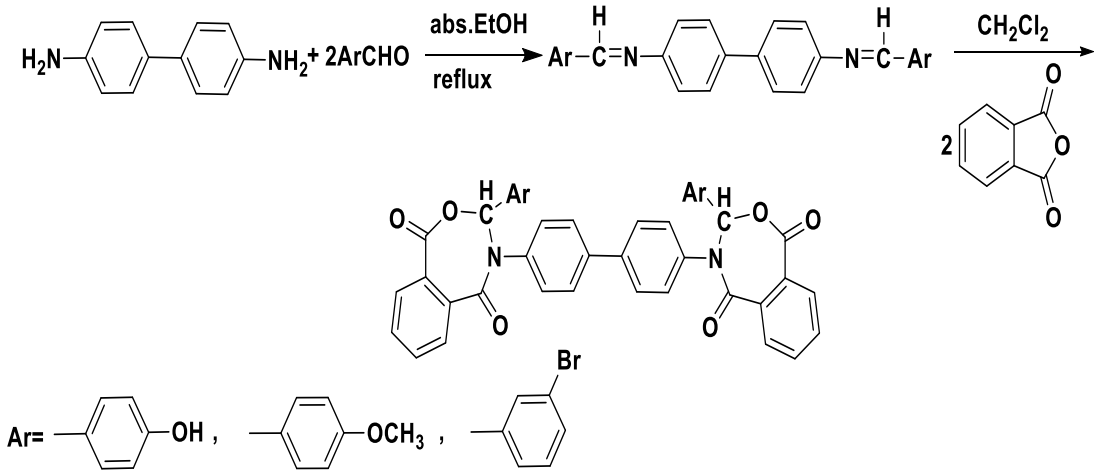
Scheme (1-11): Synthesis of 1,3-oxazepines through addition of maleic anhydride to imines under variable microwave power

[S. A. Yousif 2013] synthesis of several Schiff bases by condensation of 6-methoxy-2-aminobenzothiazole with some aldehydes and ketones (2-hydroxylbenzaldehyde,4-hydroxylbenzaldehyde,4-N,N–dimethyl aminoacetophenone, benzophenone) to obtain Schiff bases which were found to react with phthalic anhydride to give 1,3-oxazepine derivatives .Scheme (1-12)



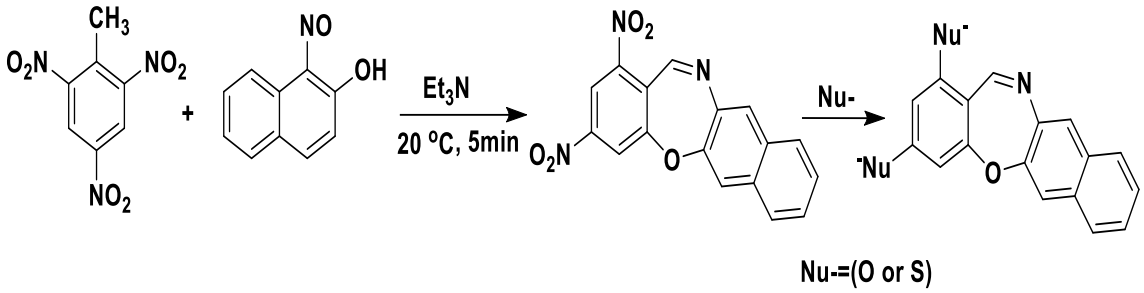
Scheme (1-12) : Formation of 1,3-oxazepine derivatives containing benzothiazole moiety

[A J.Mahrath *et.al.*,2013]synthesized new bis- 1,3 oxazepine 4,7- dione derivatives via [2+5] cycloaddition of phthalic anhydride to imines. Scheme (1-13)



Scheme (1-13) : Formation of 1,3-oxazepine derivatives containing benzothiazole moiety

Synthesized of benzo naphthol [1,4] oxazepines [A.V.Samet *et.al.*,2008] . from TNT(tetra-nitro toluene) as shown in Scheme (1-14)



Scheme (1-14): Synthesis of benzo ,naphthol ,[1,4] oxazepanes from TNT

1.7-Aims of the Work

1-To synthesize and identify the new heterocyclic compounds containing 1,3-oxazepine.

2- Preparation of a new organic ligands that includes a β-lactam ring.

3- Preparation of complexes from reaction of prepared ligands with some metal ions.

4- Characterization of prepared ligands and their metal complexes by many physical measurements (M.P , Solubility , Color)

5- Measuring the biological activity of the prepared compounds and study of the inhibitory action of prepared ligands and their complexes.

Chapter two

Experimental part

2.1.Chemical Reagents:-

The used chemicals with their molecular formula, suppliers and degree of purity are shown in table (2-1).

Table(2-1) Chemicals used, their molecular formula, and degree of purity

NO.	Material	Molecular Formula	Company	Purity
1	6-Amino Penicillinic Acid	$C_6H_{12}O_3N_2S$	Sigma-Aldrich	99.98%
2	Pyridine	C_5H_5N	Sigma-Aldrich	98%
3	Zinc Chloride	$ZnCl_2$	BDH	98%
4	n-Butyl aldehyde	C_4H_8O	BDH	98%
5	Crotone aldehyde	C_4H_6O	BDH	98%
6	Terephthalaldehyde	$C_8H_6O_2$	Sigma-Aldrich	99%
7	Furfuraldehyde	$C_5H_4O_2$	Sigma-Aldrich	97%
8	Absolute Ethanol	C_2H_6O	BDH	99%
9	Benzene	C_6H_6	BDH	99%
10	Diethyl ether	$(C_2H_5)_2O$	BDH	99.5%

11	**benzaldehyde**	**C_7H_6O**	**BDH**	**99.5%**
12	**phthalic anhydride**	**$C_8H_4O_3$**	**Alpha**	**99.5%**
13	**Succinic anhydride**	**$C_4H_4O_3$**	**Alpha**	**99.5%**
14	**Maleic anhydride**	**$C_4H_2O_3$**	**Alpha**	**99.5%**
15	**Mueller-Hinton Agar**		**Difco(U.S.A)**	**99%**

2.2. Instrument Analysis and Equipment:-

2.2.1.Melting Points Apparatus

Melting points were determined using SMP30 melting point apparatus and are uncorrected; College of Science for Women, University of Babylon.

2.2.2.Fourier Transform Infrared Spectra (FT-IR)

The FT-IR spectra were obtained as KBr discs using a Biotic 600 FT-IR spectrophotometer in the range 400-4000 cm^{-1}. Which, were recorded at the College of Science for Women University of Babylon.

2.2.3 . Conductivity Measurements

Electrical conductivity measurements of the complexes were made with absolute (DMSO) at 25 ºC using WTW Cond 7300 digital conductivity meter at College of, Science for Women, Department of Chemistry, University of Babylon.

2.2.4.UV-Visible Spectra Measurements

UV-visible spectra of prepared ligand solutions and their complexes were recorded in ethanol absolute. At College of Science for Women, University of Babylon.

2.2.5. (^{1}H, ^{13}C) NMR Spectra Measurements

The nuclear magnetic resonance spectra were measured at Isfahan University of Technology (IUT) Iran using an instrument Bruker ^{1}HNMR at (400mHz) and ^{13}C NMR Switzerland with (DMSO).

2.2.6. Flame Atomic Absorption Spectroscopy

The atomic absorption analysis was used to determine the metal contents by Perkin Elmer,1100B,Atomic Absorption Spectrophotometer at BPC Analysis Center in Baghdad.

2.2.7.Mass Spectrometric

The spectra measured by Agilent Technology (HP), Model: 5973 Network Mass Selective Detector, at Isfahan University of Technology (IUT) .

2.2.8.Rotary evaporator

Laborota 4000 efficient Heidolph (Germany)at Chemistry Department /College of Science for Women, University of Babylon.

2.2.9.Differential Thermal Gravimeter (DTG)-60 Shimadzu (Japan)

At Chemistry Department /College of Science for Women, University of Babylon.

2.3. Synthesis of Schiff's base

X1: General Procedure of Schiff's base Ligand

The ligands were synthesized by dissolving of 6-Aminopenicillanic acid (1eq.) in 35ml absolute ethanol with basic medium from pyridine and then add (1eq.) of an aldehyde. The mixture was refluxed for 5hrs, then the solution was dried by rotary evaporator to afforded the crud Schiff's base which recrystallized by absolute ethanol. All ligands were synthesized in same ratio from (1:1) (amine: aldehyde) except the Terephthaldehyde which was (1:2) (Terephthaldehyde : 6-Aminopenicillinic acid).

2.3.1. 6-(Butylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid(L1)

General procedure **(X1)** was followed using 6-Aminopenicillanic acid (0.0231 mol, 5 gm) and n-butylaldehyde (0.0231 mol, 2.102 ml), to afforded **L1** (4.3gm, 86%); as an yellow powder; M.P = 206-209^{o} C.

2.3.2. 6-(But-2-1-ylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid(L2)

General procedure **(X1)** was followed using 6-Aminopenicillanic acid (0.0231 mol, 5 gm) and (0.0231 mol, 1.913ml) of (Crotone aldehyde), to afforded **L2** (4.5gm, 90%); as an brown color powder; M.P =215-220^{o} C.

2.3.3. 6,6'-((1,4-Phenylenebis(methaneylylidene))bis(azaneylylidene))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid)(L3)

General procedure **(X1)** was followed using (2mole) 6-Aminopenicillanic acid (0.0231 mol, 10 gm) and terephthalaldehyde (0.0231 mol, 3.098gm), to afforded **L3** (8.5gm, 85%), as an orange color powder; M.P =260-264^{o} C.

2.3.4. 6-((Furan-2-ylmethylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid (L4)

General procedure **(X1)** was followed using 6-Aminopenicillanic acid (0.0231 mol, 5 gm) and furfuralaldehyde (0.0231 mol, 1.915ml), to afforded **L4** (4.6gm,92%), as an glossy black color powder; M.P = 212-215^{o} C.

2.3.5.6-(Benzylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid(L5)

General procedure **(X1)** was followed using 6-Aminopenicillanic acid (0.0231 mol, 5 gm) and benzaldehyde (0.0231 mol, 2.453ml), to afforded **L5** (3.9)gm,92%), as an orange color powder; M.P = 132-134℃ [B. Q . Ali *et.al*.,(2016)]

2.4. Synthesis of Schiff's bases complex

X2 General Procedure of schiff's base complex

Mixed the (L1, L2, L4) with (Zn) ratio from (2:1) mole respectively except (L3) ratio from (1:1) and add 15 ml of absolute ethanol. The mixture was refluxed for 3h, then cooled to room temperature, the colored complexes got precipitated slowly and recrystallized from absolute ethanol.

2.4.1.[Bis (6-(butylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid) dichlorozinc(II)] (B1)

General procedure **(X2)** was followed using (0.00185mol , 0.5gm) of (L1) with $ZnCl_2$ (0.000925mol , (0.126gm), to afforded **B1** (0.35gm,70%), as an pale yellow color powder; M.P = 215-218^{o} C.

2.4.2.[Bis(6-(but-2-1-ylideneamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid)dichlorozinc(II)] (B2)

General procedure **(X2)** was followed using (0.00186mol , 0.5gm) of (L2) with $ZnCl_2$ (0.000932mol , (0.127gm), to afforded **B2** (0.39gm,78%); as an light brown color powder; M.P =257-260^o C.

2.4.3.[(6,6'-((1,4-Phenylenebis(methaneylylidene)) bis (azaneylylidene))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid) dichlorozinc(II)] (B3)

General procedure **(X2)** was followed using (0.00094 mol, 0.5gm) of (L3) with $ZnCl_2$ (0.00094mol, 0.128gm), to afforded **B3** (0.41gm, 82%), as an light orange color powder; M.P = 273-277^o C.

2.4.4.[Bis(6-((furan-2-ylmethylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid)dichlorozinc(II)] (B4)

General procedure **(X2)** was followed using (0.00169 mol, 0.5gm) of (L4) with $ZnCl_2$ (0.000849 mol, 0.1157gm), to afforded **B4** (0.44gm, 88%), as an black color powder; M.P = 218-221^o C.

2.5. Synthesis of 1,3-Oxazepine's derivatives

X3 General Procedure of 1,3-Oxazepine's derivatives

An appropriate equal moles of Schiff bases with anhydride (except Schiff bases of terephthalaldehyde ratio from 1mol shiff base to 2mol anhydride) were dissolved in dry benzene (150 ml). The reaction mixture was refluxed for overnight and then the solution was concentrated under rotary evaporator. The residue was triturated in diethyl ether, filtered and dried to obtain the target compounds.

2.5.1.6-(4,7-Dioxo-2-phenyl-1,3-oxazepan-3-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0]heptane-2-carboxylic acid (C1)

General procedure **(X3)** was followed using (1gm, 0.00328mol) of Schiff base from benzaldehyde **(L5)** with succinic anhydride (0.35gm, 0.00328mol), to afforded **C1** (0.67gm, 67%), as an light-yellow color powder; M.P = 190-194º C.

2.5.2.6-(1,5-Dioxo-3-phenylbenzo[e][1,3]oxazepin-4(1*H*,3*H*,5*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (C2)

General procedure **(X3)** was followed using (1gm,0.00328mol) of Schiff base from benzaldehyde **(L5)** with phthalic anhydride (0.486gm, 0.00328mol), to afforded **C2** (0.64gm,64%), as an pale-yellow color powder; M.P = 201-205º C.

2.5.3.6-(4,7-Dioxo-2-phenyl-1,3-oxazepin-3(2*H*,4*H*,7*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (C3)

General procedure **(X3)** was followed using (1gm,0.00328mol) of Schiff base from benzaldehyde **(L5)** with maleic anhydride (0.322gm, 0.00328mol), to afforded **C3** (0.63gm, 63%), as a yellow color powder; M.P = 183-186º C.

2.5.4.6,6'-(2,2'-(1,4-Phenylene)bis(4,7-dioxo-1,3-oxazepane-3,2-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) (C4)

General procedure **(X3)** was followed using (1gm, 0.00188mol) of Schiff base from terephthalaldehyde **(L3)** with succinic anhydride (0.376gm, 0.00376mol), to afforded **C4** (0.83gm,80%), as an orange color powder; M.P = 142-145º C.

2.5.5.6,6'-(3,3'-(1,4-Phenylene)bis(1,5-dioxobenzo[e][1,3]oxazepine-4,3(1*H*,3*H*,5*H*)-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) (C5)

General procedure **(X3)** was followed using (1gm, 0.00188mol) of Schiff base from terephthalaldehyde **(L3)** with phthalic anhydride (0.556gm, 0.00376mol), to afforded **C5** (0.87gm,87%), as an light nutty color powder; M.P = 149-153^{o} C.

2.5.6.6,6'-(2,2'-(1,4-Phenylene)bis(4,7-dioxo-1,3-oxazepine-3,2(2*H*,4*H*,7*H*)-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) (C6)

General procedure **(X3)** was followed using (1gm, 0.00188mol) of Schiff base from terephthalaldehyde **(L3)** with maleic anhydride (0.368gm,0.00376mol), to afforded **C6** (0.85gm,85%), as an nutty color powder; M.P = 128-130^{o} C.

2.5.7.6-(2-(Furan-2-yl)-4,7-dioxo-1,3-oxazepan-3-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (C7)

General procedure **(X3)** was followed using (1gm, 0.00339 mol) of Schiff base from furfural **(L4)** with succinic anhydride (0.368gm, 0.00339mol), to afforded **C7** (0.81gm,81%), as an gray color; M.P = 163-165^{o} C.

2.5.8.6-(3-(Furan-2-yl)-1,5-dioxobenzo[e][1,3]oxazepin-4(1*H*,3*H*,5*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (C8)

General procedure **(X3)** was followed using (1gm, 0.00339mol) of Schiff base from furfural **(L4)** with phthalic anhydride (0.502gm, 0.00339mol), to afforded **C8** (0.79gm,79%), as an gray color powder; M.P = 171-176^{o} C.

2.5.9.6-(2-(Furan-2-yl)-4,7-dioxo-1,3-oxazepin-3(2*H*,4*H*,7*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (C9)

General procedure **(X3)** was followed using (1gm, 0.00339mol) of Schiff base from furfural **(L4)** with maleic anhydride (0.332gm, 0.00339mol), to afforded **C9** (0.85gm, 85%), as an gray color powder; M.P = 158-160^{o} C.

2.6. Synthesis of 1,3-Oxazepine's derivative complex

X4 General Procedure 1,3-Oxazepine's derivative complex

Mixed the **(C1,C2,C3,C7,C8,C9)** with (Zn) ratio from (2:1) mole, respectively, except **(C4,C5,C6)** ratio from (1:1) and add 15 ml of absolute ethanol. The mixture was refluxed for 3h, then cooled to room temperature, the colored complexes were precipitated slowly and recrystallized from absolute ethanol.

2.6.1.[(4,7-Dioxo-2-phenyl-1,3-oxazepan-3-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) dichlorozinc(II)] (D1)

General procedure **(X4)** was followed using (0.00123mol, 0.5gm) of **(C1)** with $ZnCl_2$ (0.000618 mol, 0.0842gm), to afforded **D1** (0.31gm, 62%), as an off white color powder ; M.P = 255-259^{o} C.

2.6.2.[(6-(1,5-Dioxo-3-phenylbenzo[e][1,3]oxazepin-4(1*H*,3*H*,5*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid) dichlorozinc(II)] (D2)

General procedure **(X4)** was followed using (0.0011mol, 0.5gm) of **(C2)** with $ZnCl_2$ (0.000552 mol, 0.0752gm), to afforded **D2** (0.37gm, 74%), as an light beige color powder; M.P = 241-244^{o} C.

2.6.3. [((4,7-Dioxo-2-phenyl-1,3-oxazepin-3(2*H*,4*H*,7*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) dichlorozinc(II)](D3)

General procedure **(X4)** was followed using (0.001241mol, 0.5gm) of **(C3)** with $ZnCl_2$ (0.000621 mol, 0.0846gm), to afforded **D3** (0.34gm, 68%), as an pale yellow color powder ; M.P = 232-235^o C.

2.6.4. [(6,6'-(2,2'-(1,4-Phenylene)bis(4,7-dioxo-1,3-oxazepane-3,2-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid)) dichlorozinc(II)] (D4)

General procedure **(X4)** was followed using (0.000729 mol, 0.5gm) of **(C4)** with $ZnCl_2$ (0.000729mol, 0.1079gm), to afforded **D4** (0.39gm, 78%), as an light orange color powder; M.P = 210-215^o C.

2.6.[(5.6,6'-(3,3'-(1,4-Phenylene)bis(1,5-dioxobenzo[e][1,3]oxazepine-4,3(1*H*,3*H*, 5*H*)-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid)) dichlorozinc(II)] (D5)

General procedure **(X4)** was followed using (0.000737mol, 0.5gm) of **(C5)** of with $ZnCl_2$ (0.000737mol, 0.1004gm), to afforded **D5** (0.42gm,84%), as an orange color powder; M.P = 241-244^o C.

2.6.6. [(6,6'-(2,2'-(1,4-Phenylene)bis(4,7-dioxo-1,3-oxazepine-3,2(2*H*,4*H*,7*H*)-diyl))bis(3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) dichlorozinc(II)] (D6)

General procedure **(X4)** was followed using (0.00079mol, 0.5gm) of **(C6)** with $ZnCl_2$ (0.00079 mol, 0.1081gm), to afforded **D6** (0.44gm,88%), as an light nutty Color powder; M.P=201-204^{o}C.

2.6.7.[(6-(2-(Furan-2-yl)-4,7-dioxo-1,3-oxazepan-3-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) dichlorozinc(II)](D7)

General procedure **(X4)** was followed using (0.00126mol,0.5gm) of **(C7)** with $ZnCl_2$ (0.00063 mol, 0.0864gm), to afforded **D7** (0.42gm, 84%), as an grey color powder; M.P = 230-232º C.

2.6.8. [(6-(3-(Furan-2-yl)-1,5-dioxobenzo[e][1,3]oxazepin-4(1*H*,3*H*,5*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylicacid) dichlorozinc(II)](D8)

General procedure **(X4)** was followed using (0.00113mol, 0.5gm) of **(C8)** with $ZnCl_2$ (0.000565mol, 0.077gm), to afforded **D8** (0.43gm,86%), as an light gray color powder; M.P = 232-236º C.

2.6.9.[(6-(2-(Furan-2-yl)-4,7-dioxo-1,3-oxazepin-3(2*H*,4*H*,7*H*)-yl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) dichlorozinc(II)] (D9)

General procedure **(X4)** was followed using (0.00127mol, 0.5gm) of **(C9)** with $ZnCl_2$ (0.000637mol,0.0862gm), to afforded **D9** (0.45gm, 90%), as an very light gray color powder; M.P = 229-233º C.

Chapter three

Results and Discussions

3.1-Schiff bases

One of the most common reactions in chemistry is the condensation of carbonyl compounds with primary amines, which results in the creation of Schiff base compounds [Lekha L, 2014]. Because of their stability in a range of oxidative and reductive circumstances, Schiff bases, like imine ligands, have played an essential role as chelating ligands in the main group and transition metal coordination chemistry[Hadi and Kareem, 2020]. Schiff bases are changing compounds that are typically bi- or tridentate ligands capable of forming extremely stable complexes with transition metals such as nickel, cadmium, cobalt, and copper, among others. Most metal chelates are more effective antimicrobial than individual ligands. Metal complexes' biological applications and chelating abilities have sparked considerable interest [da Silva *et.al*., 2011]. Metal complexes have been widely investigated due to their various biological applications in pharmacological areas, Metal complexes having N, O as their donor atoms are very noticeable because of their important biological activities such as anticancer, and herbicidal activity [Jabbi, Husaini and Aliyu, 2020]

3.2. Solubility and Physical properties of compound:

Using various solvents, the solubility of the obtained ligands as derivatives of 6-aminopencillanic acid and its complexes formed by transitional metal ion [Zn(II)] was investigated. The results in Table (3.1) demonstrated that the ligands and all of their complexes are insoluble in water. They are also weakly soluble in a wide range of organic solvents, including methanol , ethanol , Hexane ,and with the exception of DMSO. As the table below shows Melting point , Yield ,and Colors both ligands and their complexes.

Table 3.1. Physical properties of the synthesized compounds (L1-B4)

Compd.	M.P (C°)	Color	Yield (%)	Solubility				
				H_2O	C_2H_6O	*DMSO*	CH_3OH	C_6H_6
L_1	206-209	yellow	86%	_	δ	+	δ	δ
L_2	215-220	Brown	90%	_	δ	+	δ	δ
L_3	260-264	Orange	85%	_	δ	+	δ	δ
L_4	212-215	Glossy black	92%	_	δ	+	δ	δ
L5	132-134	Orange	92%	_	δ	+	δ	δ
B_1	215-218	Pale yellow	70%	_	δ	+	δ	δ
B_2	257-260	Light brown	78%	_	δ	+	δ	δ
B_3	273-277	Light orange	82%	_	δ	+	δ	δ
B_4	218-221	black	88%	_	δ	+	δ	δ

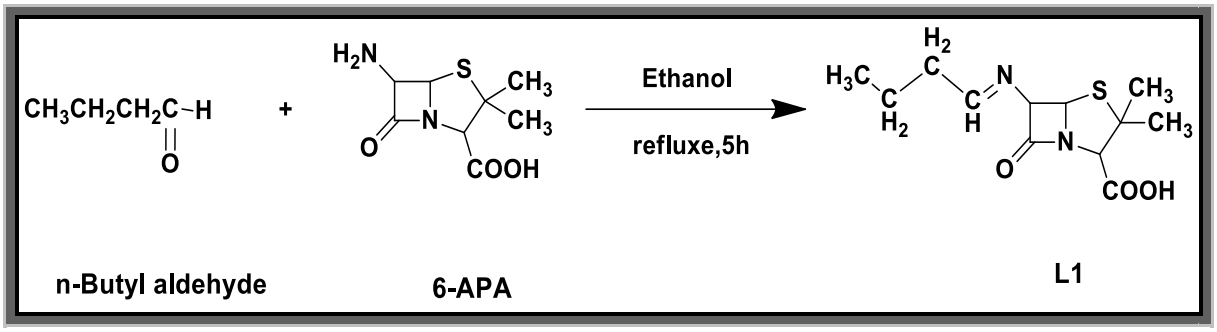
δ partial soluble

3.3.Synthesis of Schiff Bases:

Schiff bases are regarded as important intermediates in the synthesis of several chemical compounds, particularly heterocyclic compounds[al Zoubi *et.al*., 2018]From 6-aminopenicillanic acid (6-APA) as a starting material, a new series of Schiff bases and associated beta-lactam derivatives were synthesized. The chemical was treated with various aldehydes to produce Schiff base derivatives[Al-Tamimi, Muslih and Thejeel, 2014].

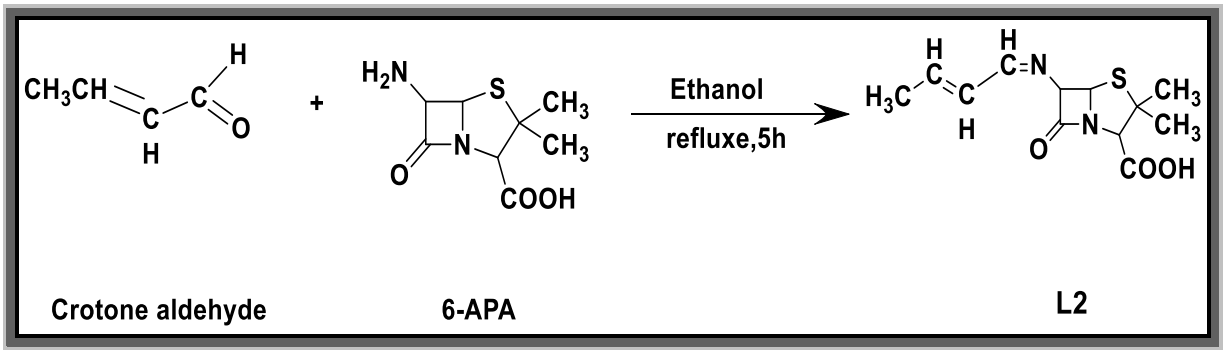
All of the Schiff base synthesized, FT-IR, ^{1}H NMR, and ^{13}C NMR spectroscopy were used to identify the compounds.

3.3.1. [6-aminopenicillanic acid (6-APA)] and n-Butyl aldehyde: L1



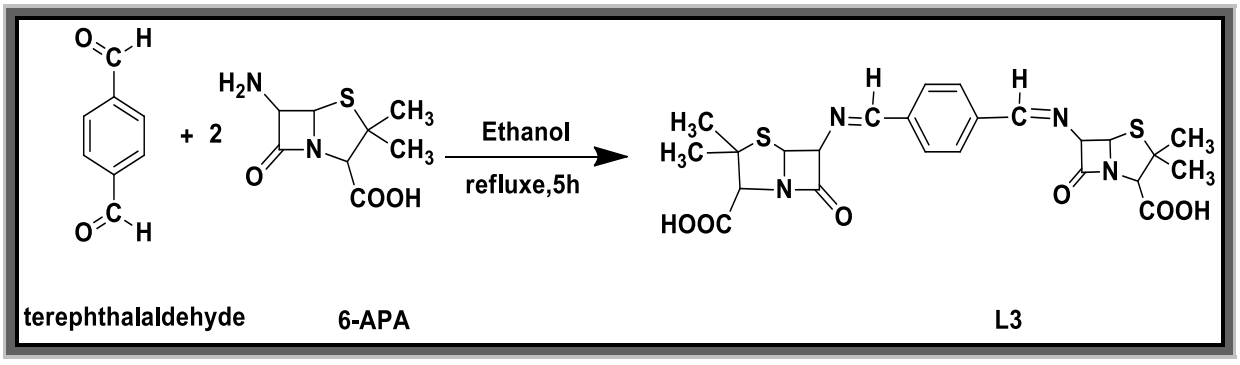
Eq.3.1.composition equation(L1)

3.3.2. [6-aminopenicillanic acid (6-APA)] and Crotonaldehyde: L2



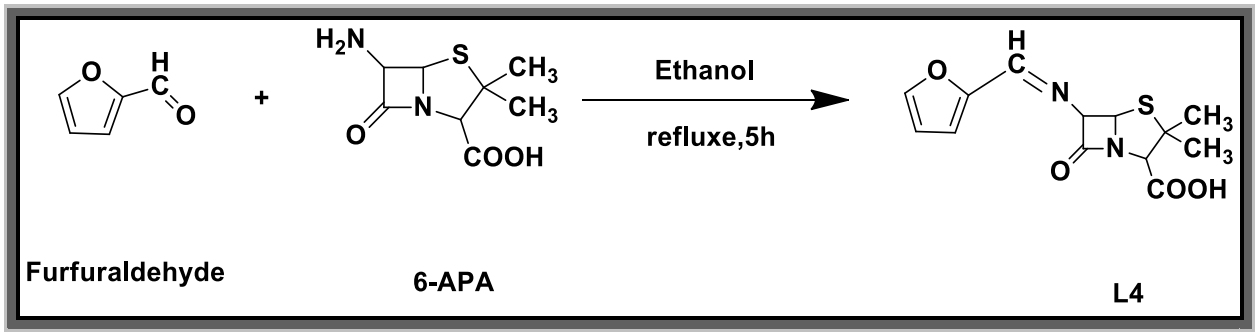
Eq.3.2.composition equation(L2)

3.3.3. [6-aminopenicillanic acid (6-APA)] and Terephthalaldehyde:L3



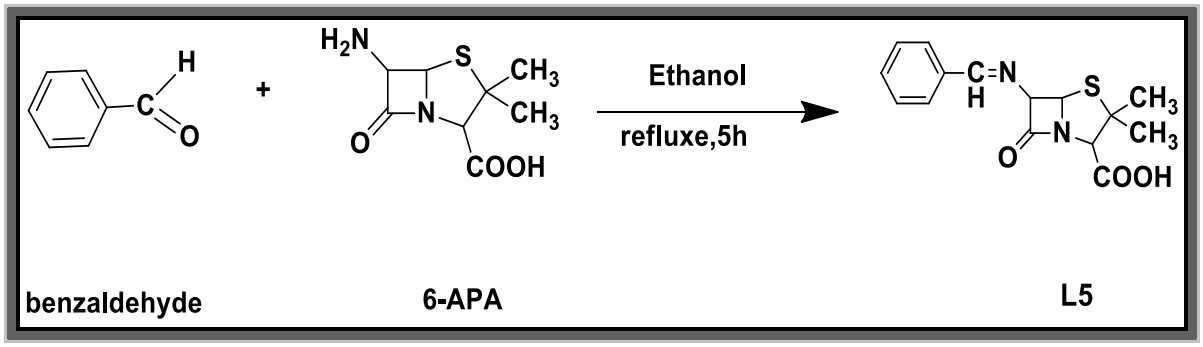
Eq.3.3.composition equation(L3)

3.3.4. [6-aminopenicillanic acid (6-APA)] and Furfural: L4



Eq.3.4.composition equation(L4)

3.3.5. [6-aminopenicillanic acid (6-APA)] and benzaldehyde: L5



Eq.3.5.composition equation(L5)

3.4. Synthesis of Schiff Bases complexes :

The reflux reaction was used to create all of the metal complexes The structure of the complexes is shown in figure below and demonstrates that the prepared ligands (L1, L2, L4, L5) are Bidentate chelating. and the preparation ratio for all complexes is 1:2, [metal: ligand][Vinusha *et al.*, 2019] ,except for (L3) complex, which is 1:1, [metal: ligand].

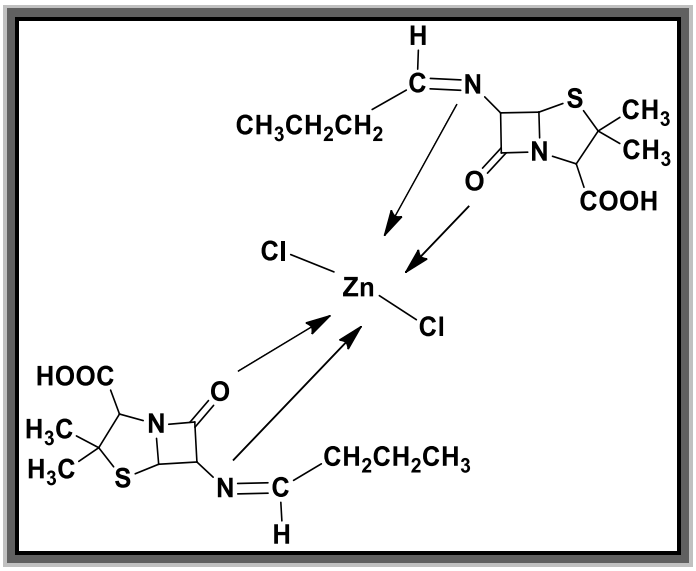


Fig.3.1. B1

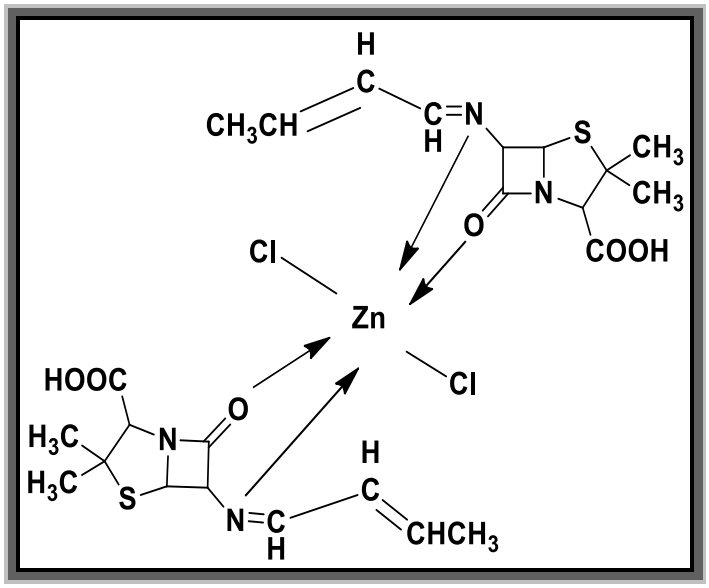


Fig.3.2. B2

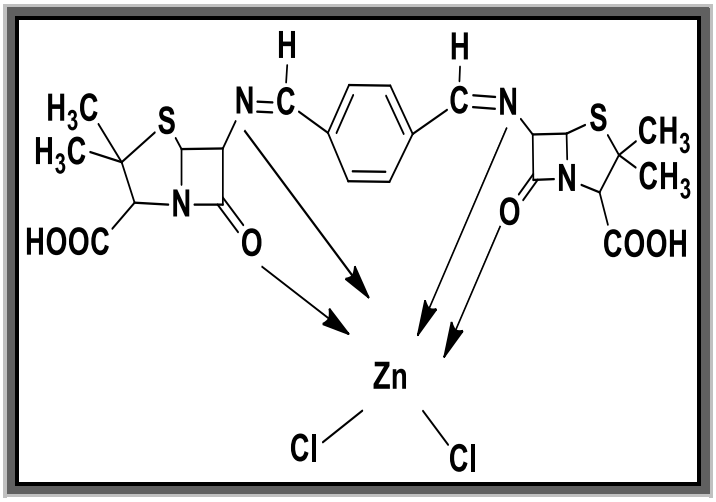


Fig.3.3. B3

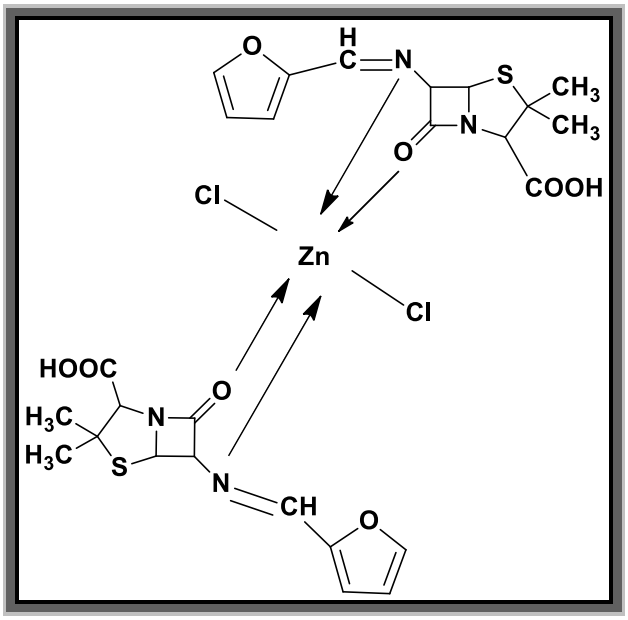


Fig.3.4. B4

3.5.FT-IR Spectra

The infrared spectrum is important in providing information about the nature and structure of functional groups because each group has its own frequency and through it can provide the initial information about the spatial shapes of the particles, as the absorption of each type of these bonds regularly gives the infrared frequency sites[Pavia, 2002].

FT-IR Spectra of Ligands (L1, L2, L3, L4, L5):

The IR spectrum of the ligands (L1, L2, L3, L4) exhibited broad band at (3117,3078,3475,3365) cm^{-1} respectively was assigned to the stretching vibration of υ(OH) group[Shakir, 2014].The IR spectrum of the ligands (L1,L2,L3,L4) band at (1772,1772,1734,1772) cm^{-1} respectively was assigned to the stretching vibration of υ(C=O) carboxyl group[Ibrahim and Sharif,2011] .The IR spectrum of the ligands (L1,L2,L3,L4) band at (1747,1734,1783,1728) cm^{-1} respectively was assigned to the stretching vibration of υ(C=O) lactam[Qusai Ali, Hamid Said and Hasan Jasim, 2016] [Fosker *et.al*., 2017].The IR spectrum of the ligands (L1, L2, L3, L4) band at (1662,1674,1662,1722) cm^{-1} respectively was assigned to the stretching vibration of υ(C=N)[Hameed, 2009]. [Aliyu and Ado, 2011]. The IR spectrum of the ligands (L2, L3, L4) band at (1627,1608,1626) cm^{-1} respectively was assigned to the stretching vibration of υ(C=C)[Güngör *et.al*.,2016].The IR spectrum of the ligand(L5) band at (1720) cm^{-1} was assigned to the stretching vibration of υ(C=O) lactam, and band at (1662) cm^{-1} to the stretching vibration of υ(C=N)[Qusai Ali, Hamid Said and Hasan Jasim, 2016].

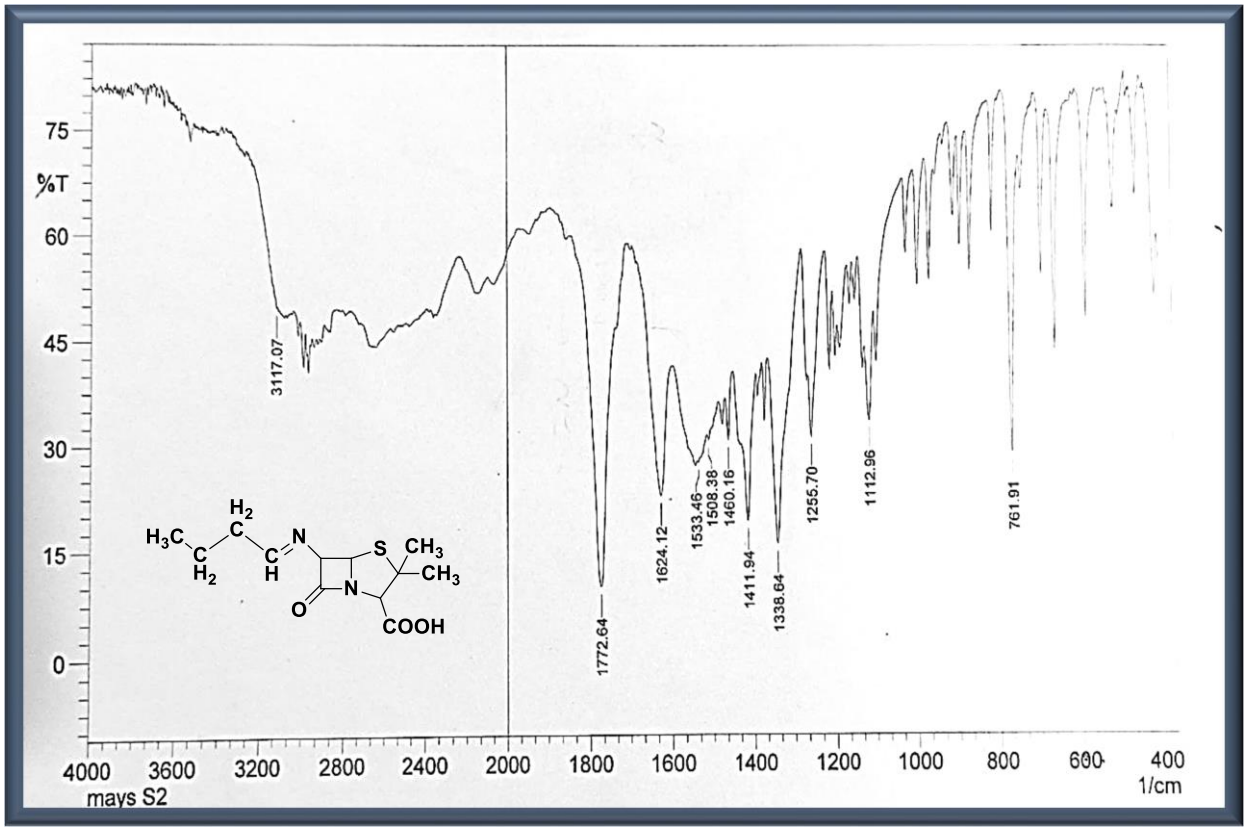


Fig (3-5): FTIR spectrum for (L1)

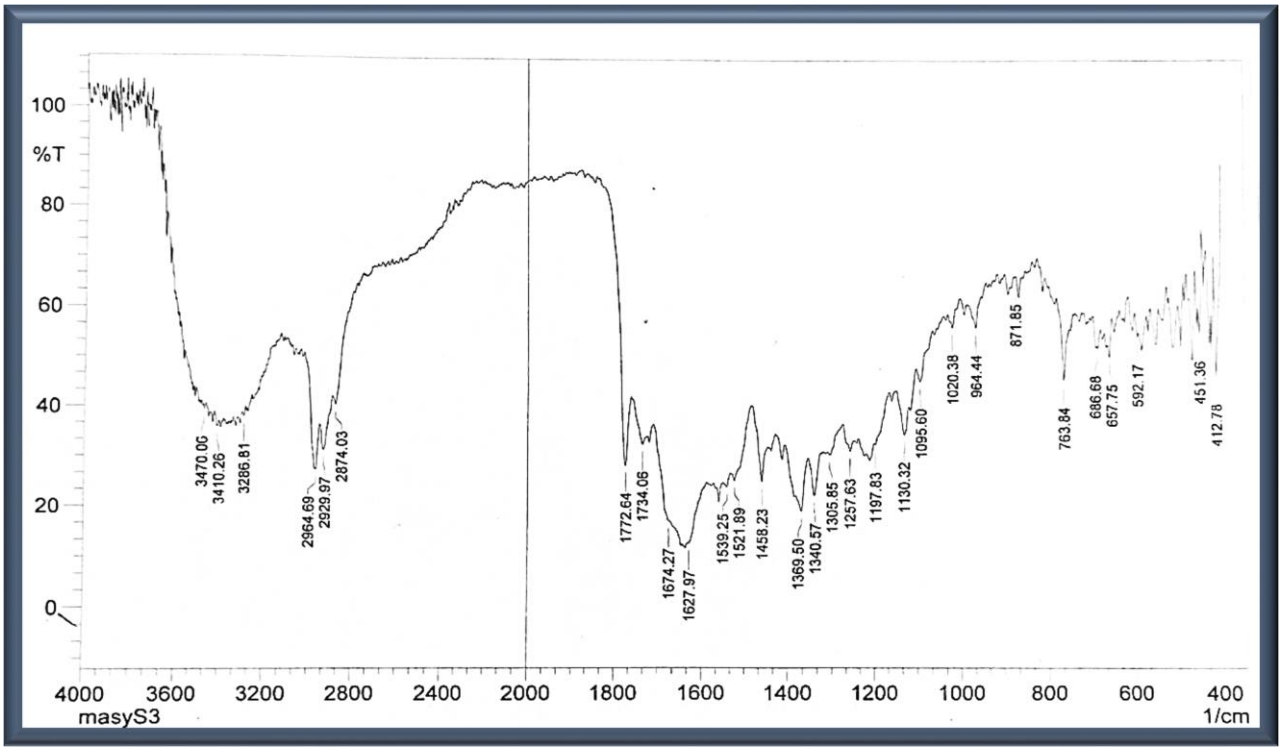


Fig (3-6): FTIR spectrum for (L2)

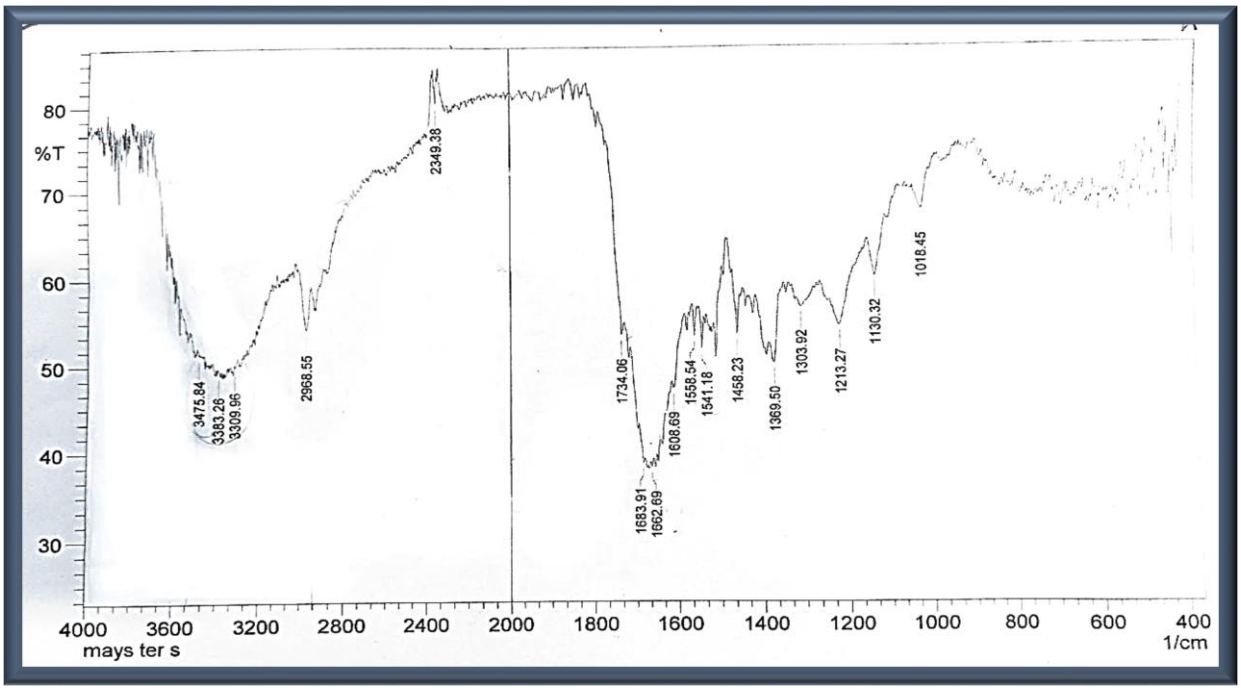


Fig (3-7): FTIR spectrum for (L3)

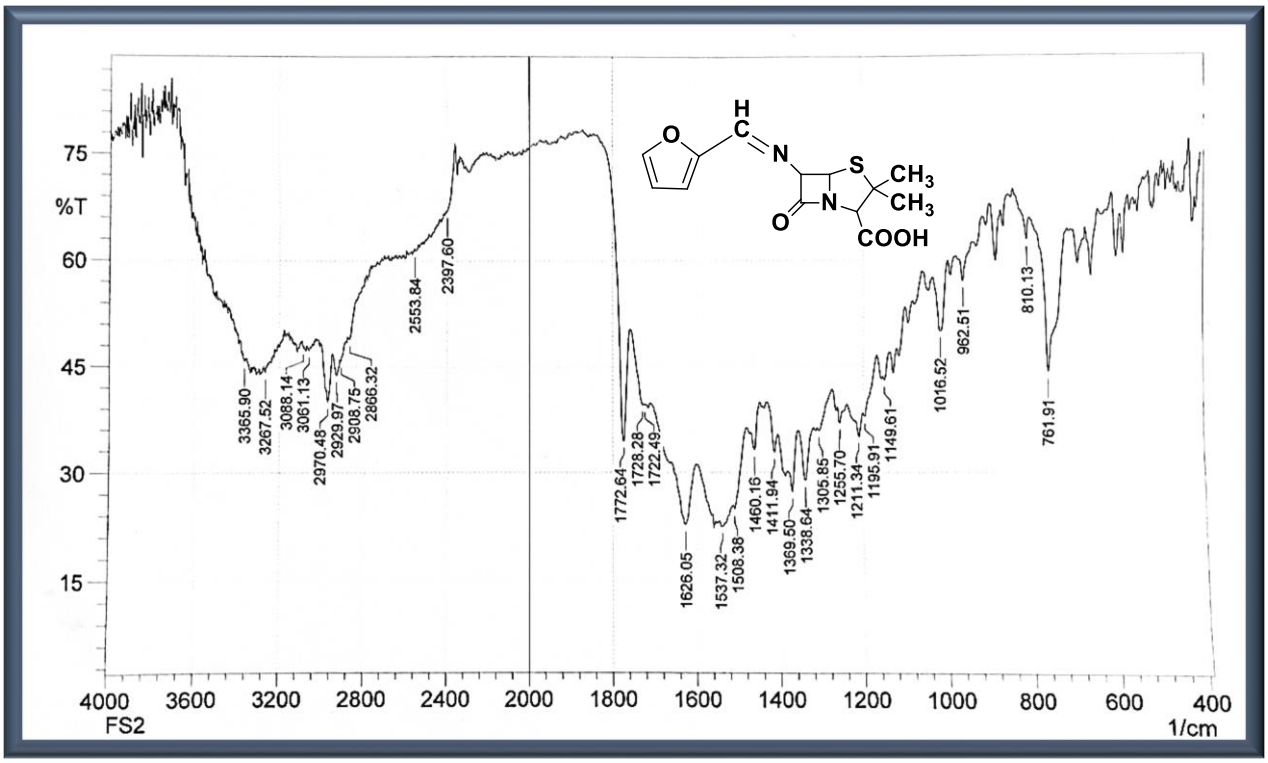


Fig (3-8): FTIR spectrum for (L4)

3.6.FT-IR Spectra of complexes (B1, B2, B3, B4):

The IR spectrum of the complexes change in this groups (C=O) lactam, and (C=N), Indicates coordination occur via the donation atom in this groups with Transition Metal Ion Zn (II),[Jaafar and Saeed, 2020].no change in this groups (O-H) and (C=C) noticed, the possibility that coordination occur via the donation atom in this group was excluded with Transition Metal Ion Zn (II), The IR spectrum of the complexes (B1, B2, B3,B4) band at (550-450) cm^{-1} was assigned to the stretching vibration of υ(M-O)and(M-N)(Vinusha *et.al.*, 2019),As shown in the Table (3.2).

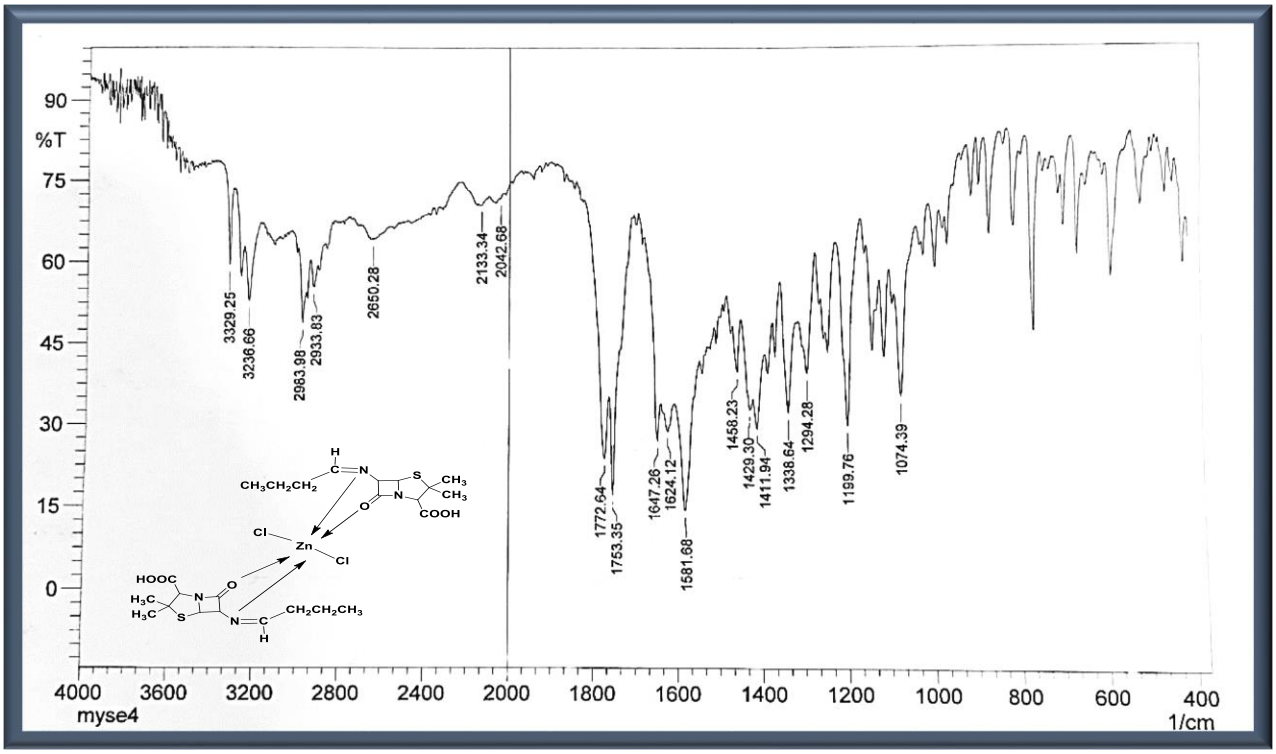


Fig (3-9): FTIR spectrum for (B1)

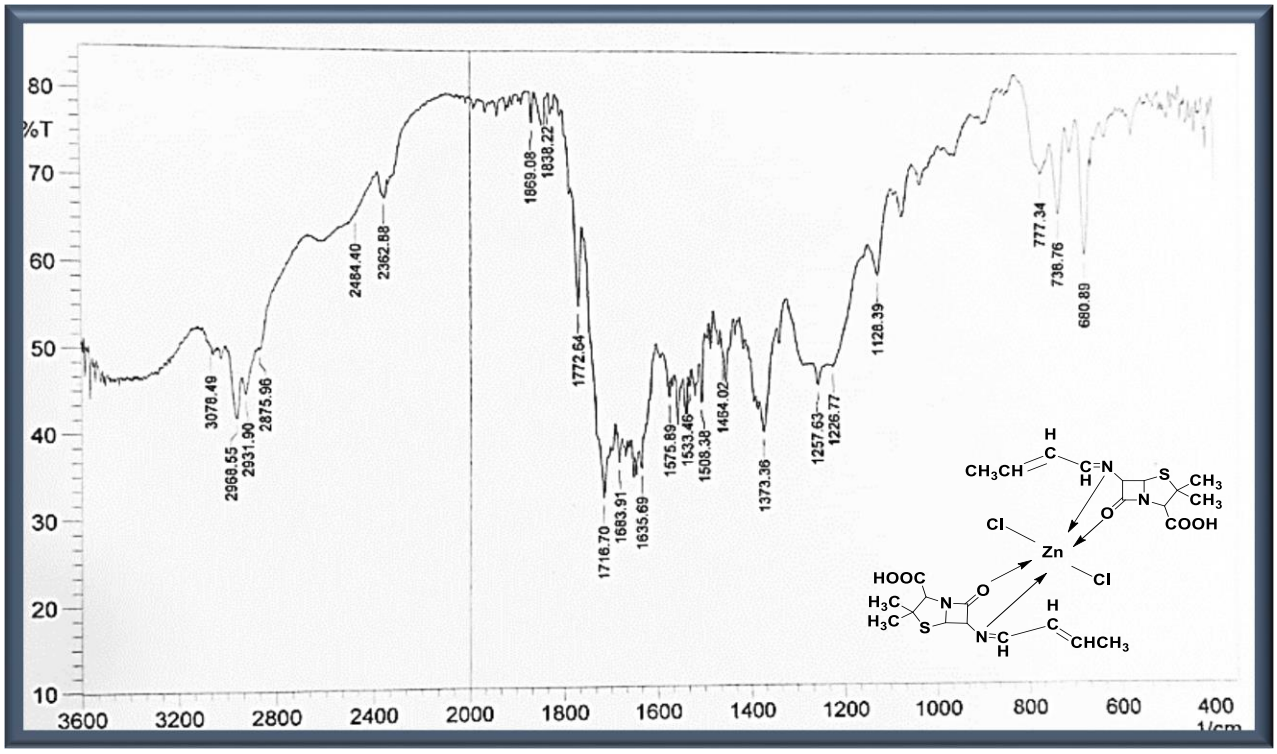


Fig (3-10): FTIR spectrum for (B2)

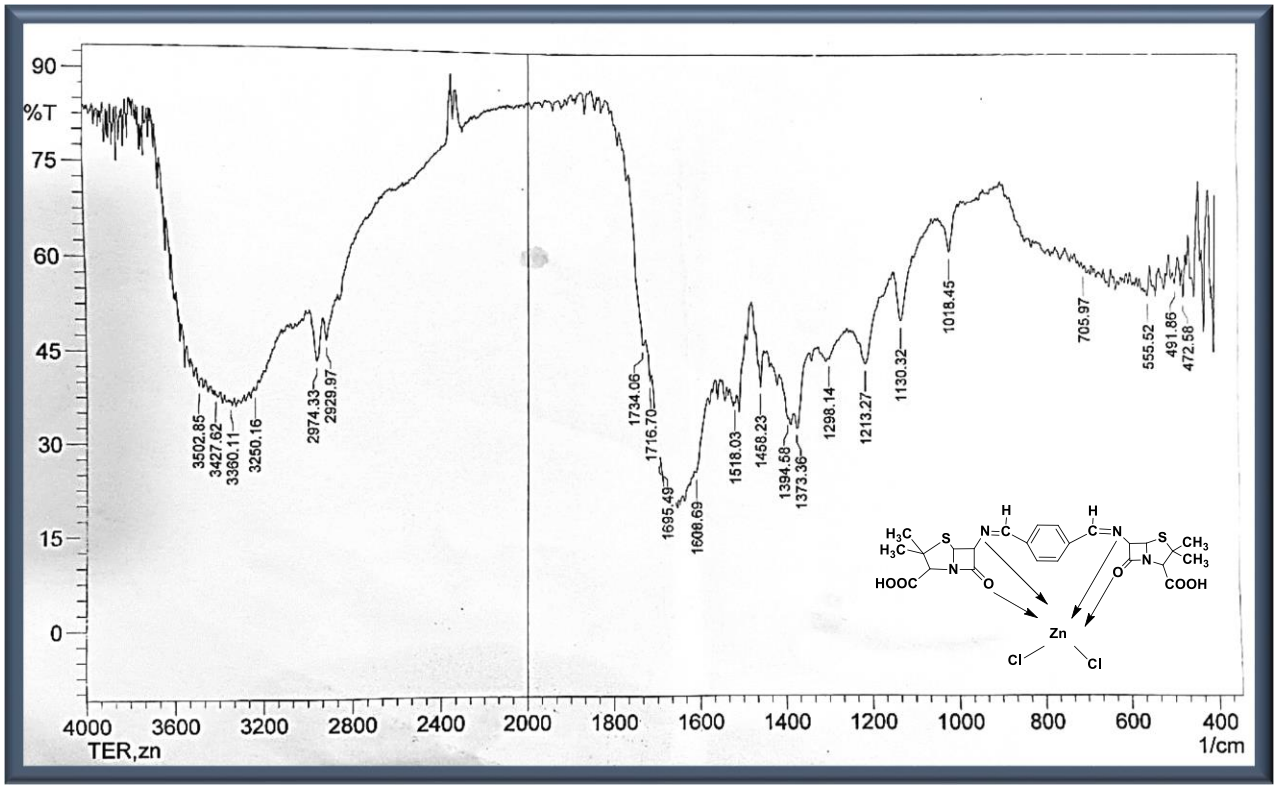


Fig (3-11): FTIR spectrum for (B3)

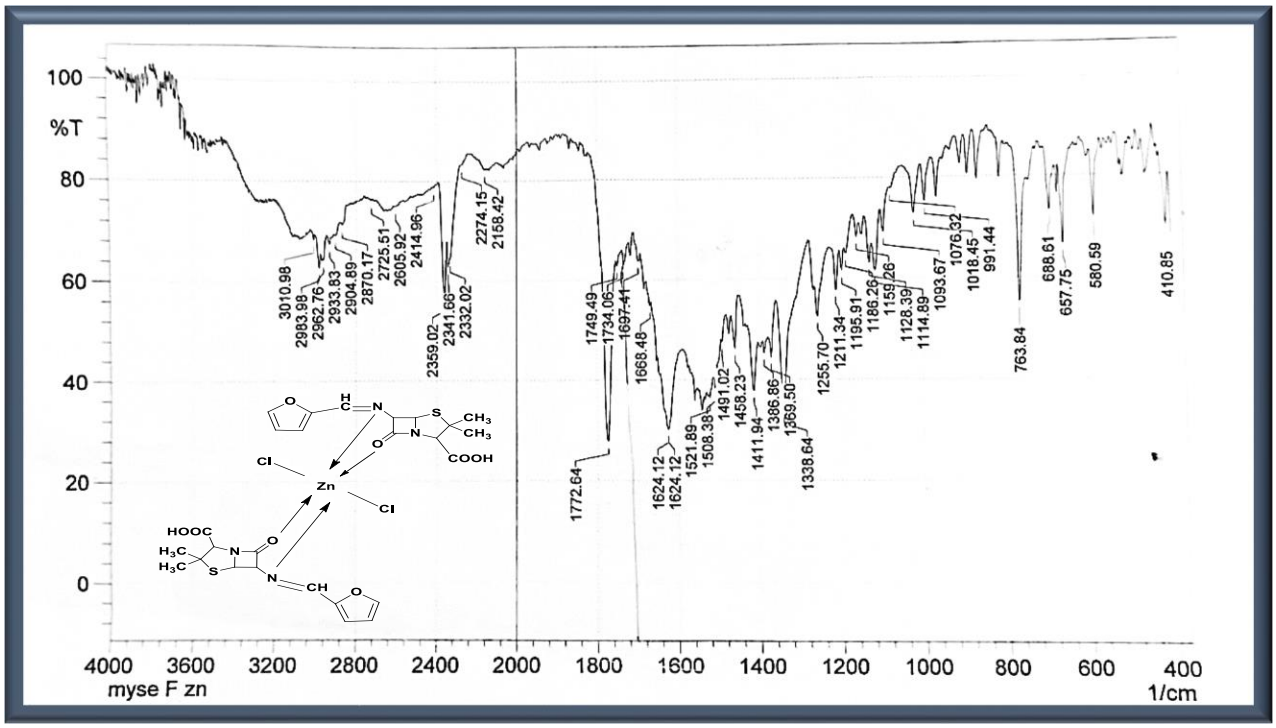


Fig (3-12): FTIR spectrum for (B4)

Table (3-2): the values of frequencies for the important bands in the infrared spectrum of the prepared complexes and the related ligand.

Compound	C=O$_{car}$	C=O$_{lact}$	C=N	C=C
L1	**1772**	**1747**	**1626**	**–**
L2	**1772**	**1734**	**1674**	**1627**
L3	**1734**	**1783**	**1662**	**1608**
L4	**1772**	**1728**	**1722**	**1626**
[Zn(L1)$_2$Cl$_2$] B1	**1772**	**1753**	**1647**	**–**
[Zn(L2)$_2$Cl$_2$] B2	**1772**	**1716**	**1683**	**1635**
[Zn(L3)Cl$_2$] B3	**1734**	**1716**	**1695**	**1608**
[Zn(L4)$_2$Cl$_2$] B4	**1772**	**1734**	**1697**	**1624**

3.7.Characterization Compounds by Mass Spectroscopy:

Mass spectrometry has been used successfully to study molecular structures [Prakash *et.al.*, 2010],The structure of substances is further supported by data collected from mass spectral analysis for further inquiry. The mass spectra for all of the target compounds (Table 3.3) show that .The computed values for the m/z ratio have been quite close to the values of Figures below represent m/z measurements.

Table 3.3. Show to fragmentation for ligand

L1		L2		L3		L4	
m/z	**Abundance**	**m/z**	**Abundance**	**m/z**	**Abundance**	**m/z**	**Abundance**
41.2	28432	41.2	254592	44.2	264192	44.1	231744
75.1	3260	75.1	971840	75.2	37288	75.1	233216
114.1	1854	114.1	685120	100.1	45456	114.1	155520
137.3	3000	137.3	72824	160.2	32088	160.1	305664
160.1	1625	160.1	140032	201.2	14672	183.2	32008
183.2	618	183.2	131712	236.2	5086	207.1	20456
216.1	617	216.1	94088	313.3	3623	216.1	16728
239.2	280	239.2	13605	423.2	463	243.2	1403
263.1	248	261.2	13697	495.5	371	281.1	4252
270.2	228	268.1	5584	530.9	180	294.9	703

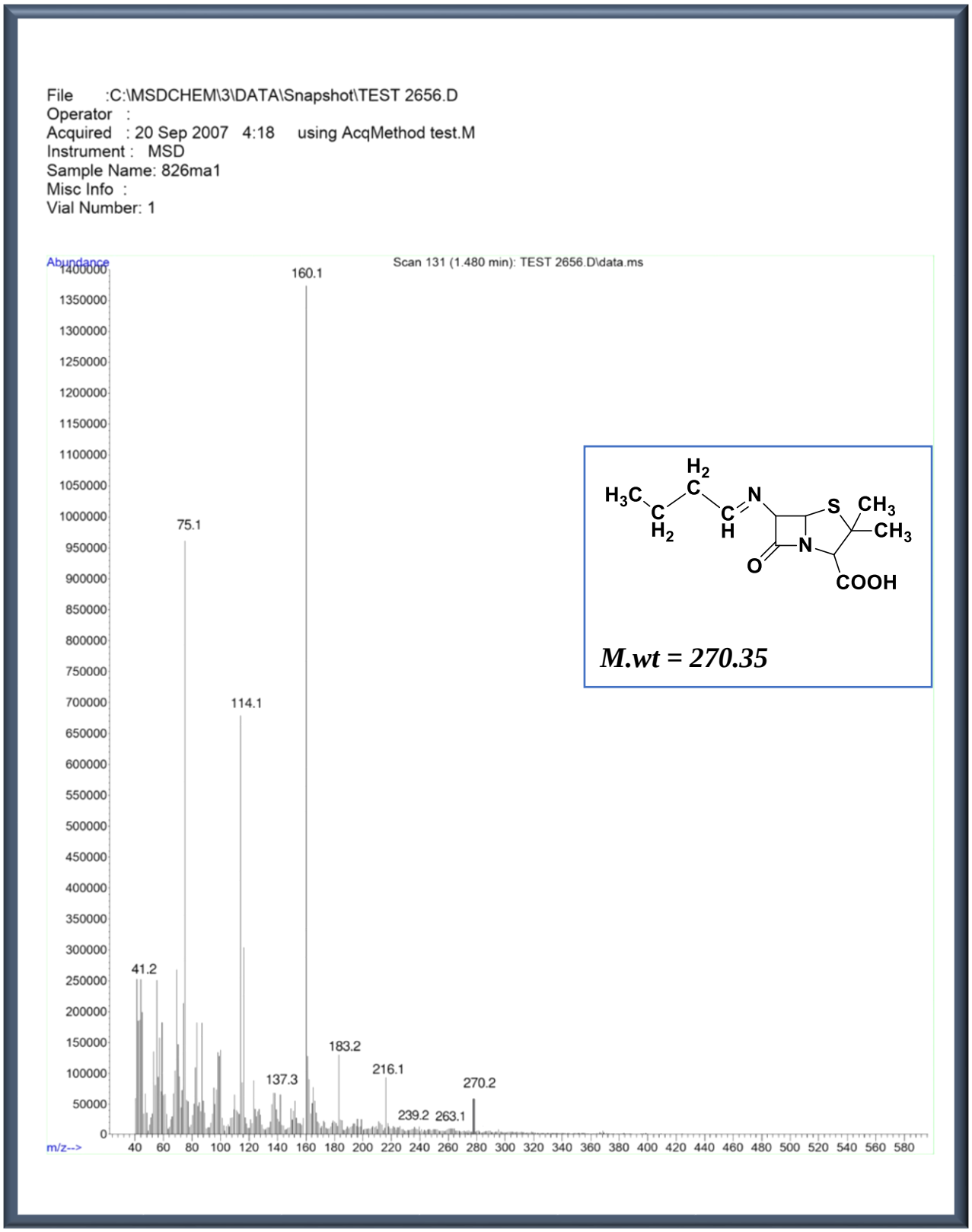


Fig. (3.13) Mass Spectra of L1

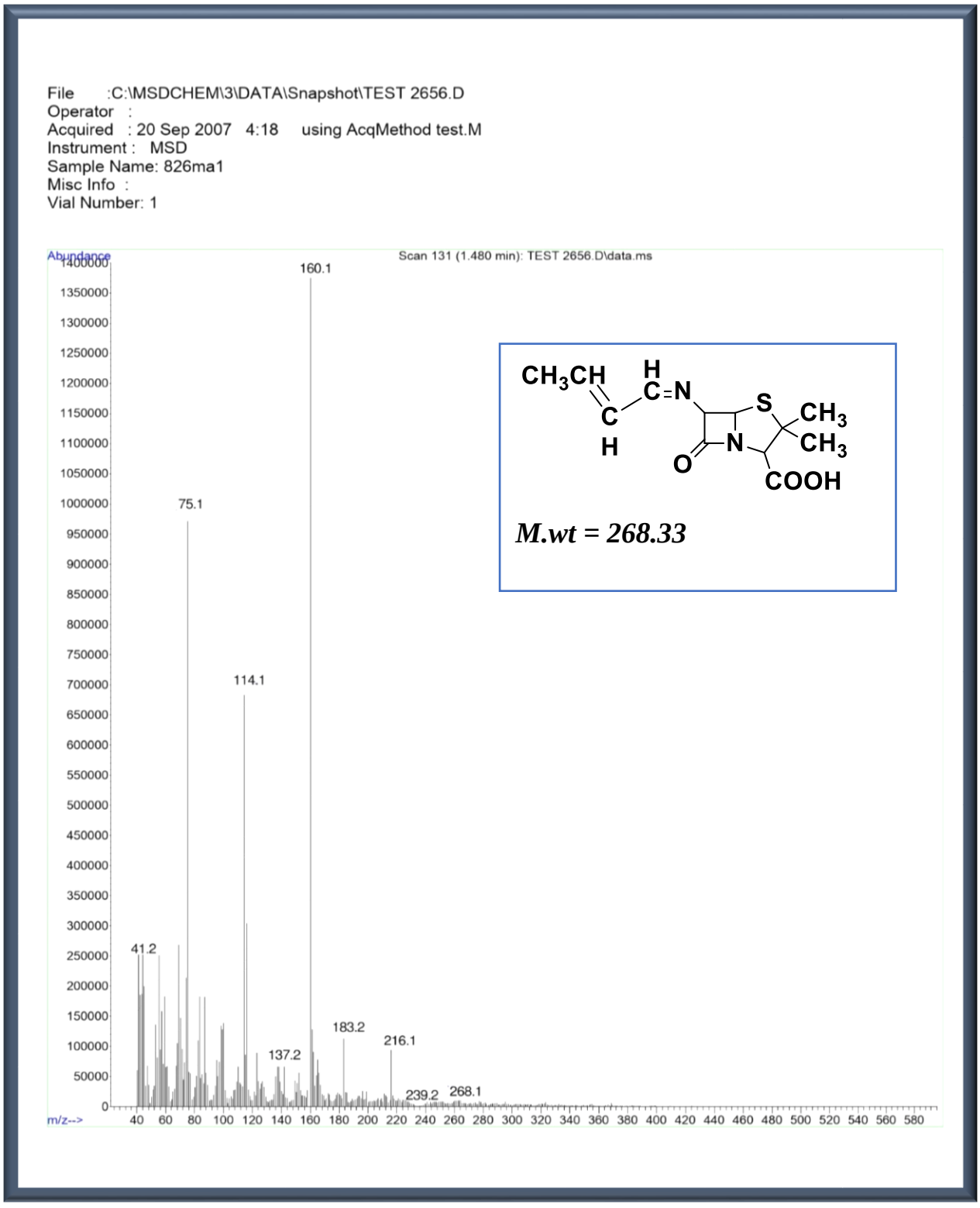


Fig. (3.14) Mass Spectra of L2

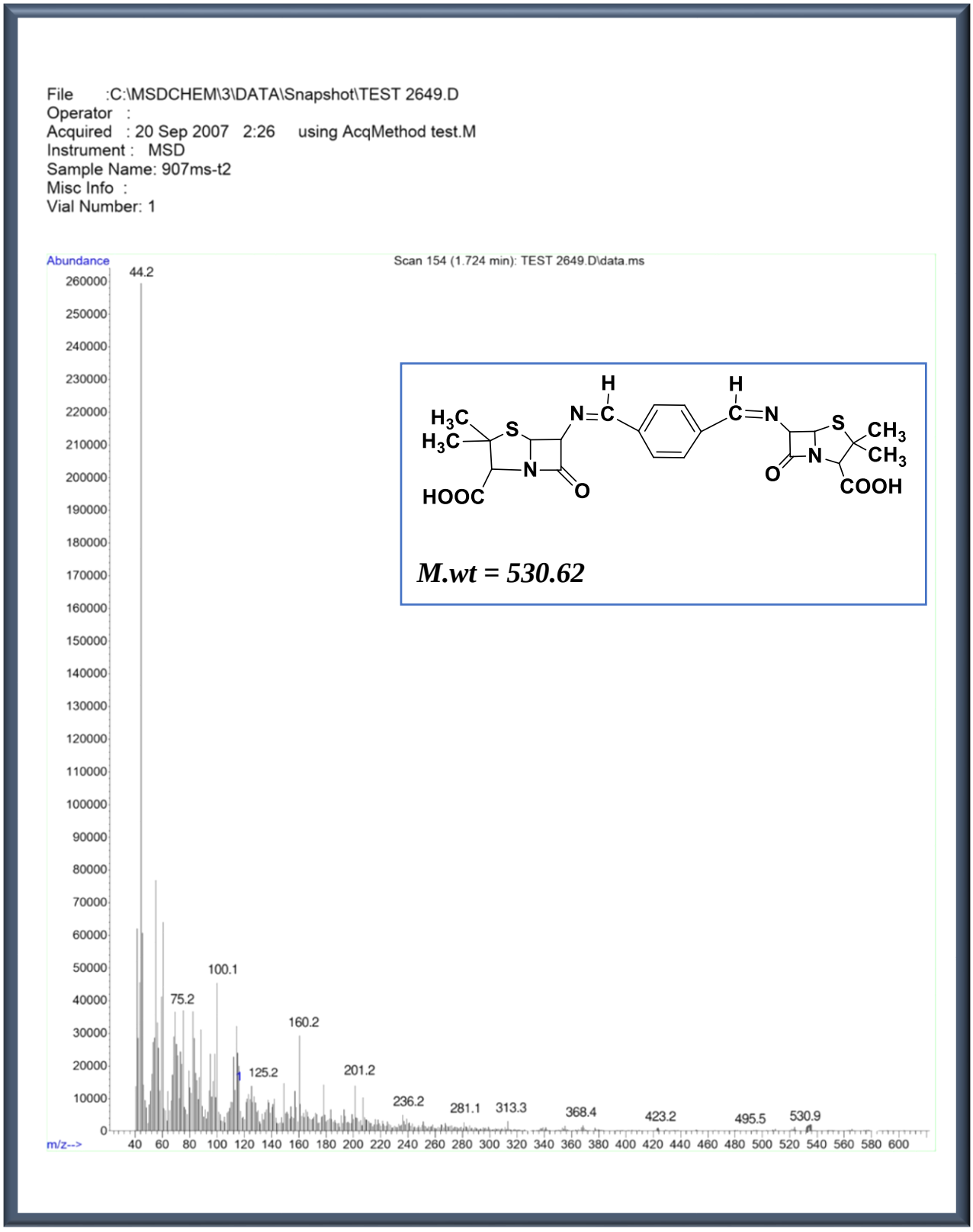


Fig. (3.15) Mass Spectra of L3

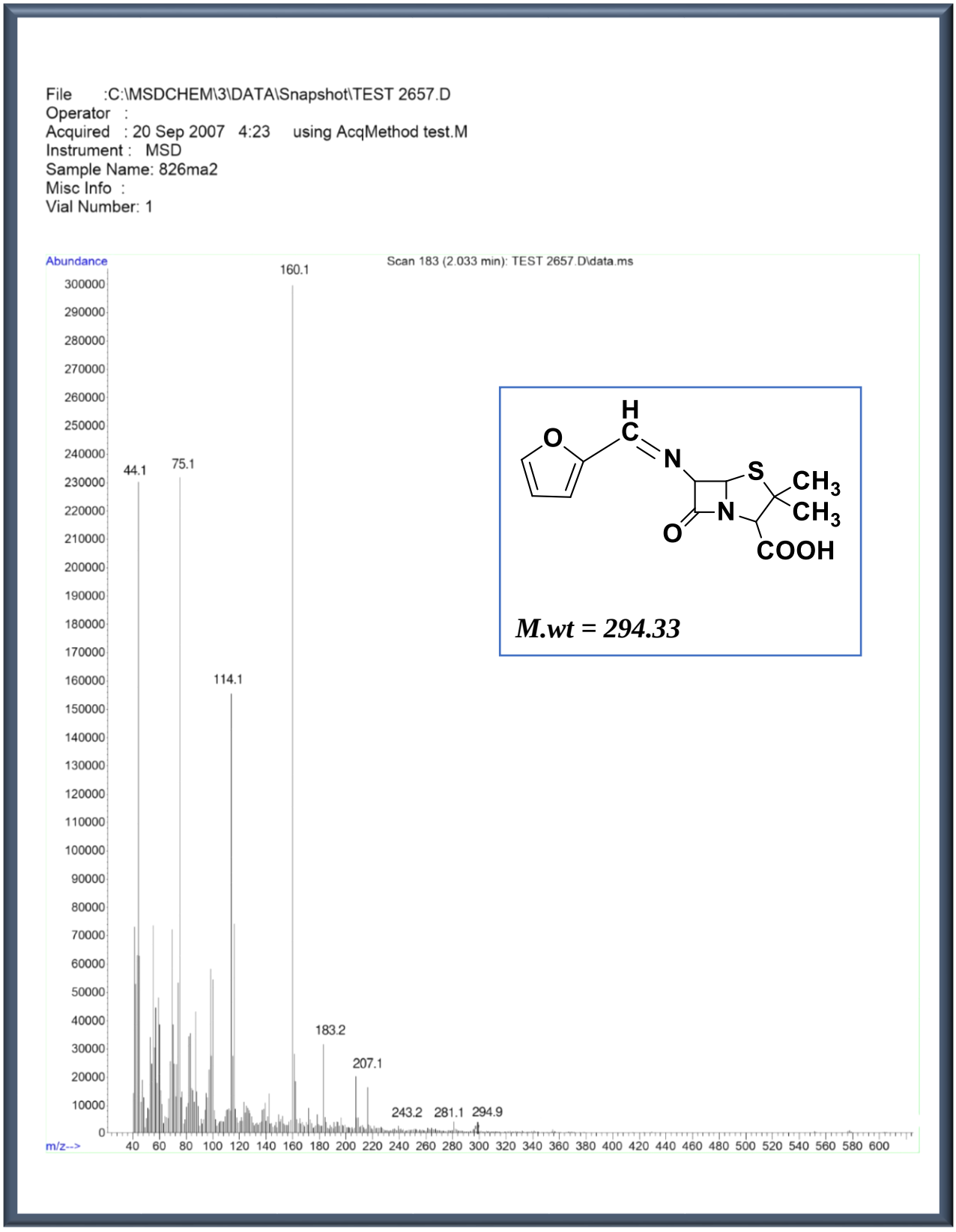


Fig. (3.16) Mass Spectra of L4

3.8.^{1}H-NMR Spectra of the Schiff base Ligand :

The 1H-NMR spectrum of the ligands figures below . The DMSO-d6 solvent was showed a signal at (2.5ppm) and the first signal at δ=(1.1-1.5)ppm due (CH_3) groups and signals in the range (4.5-4.8) ppm to the proton of the carbon atom bearing the carboxylic group, The other signals at δ=(7.6,7.4,8.5,7.5)ppm[Karaoğlan, Avcıata and Gül, 2007], due to the (N=CH) group of (L1,L2,L3,L4) respectively, and the signals at δ=(11.19,11.27,11.21,11.4)ppm due (OH) groups of(L1,L2,L3,L4) respectively[Jasim et.al., 2020].

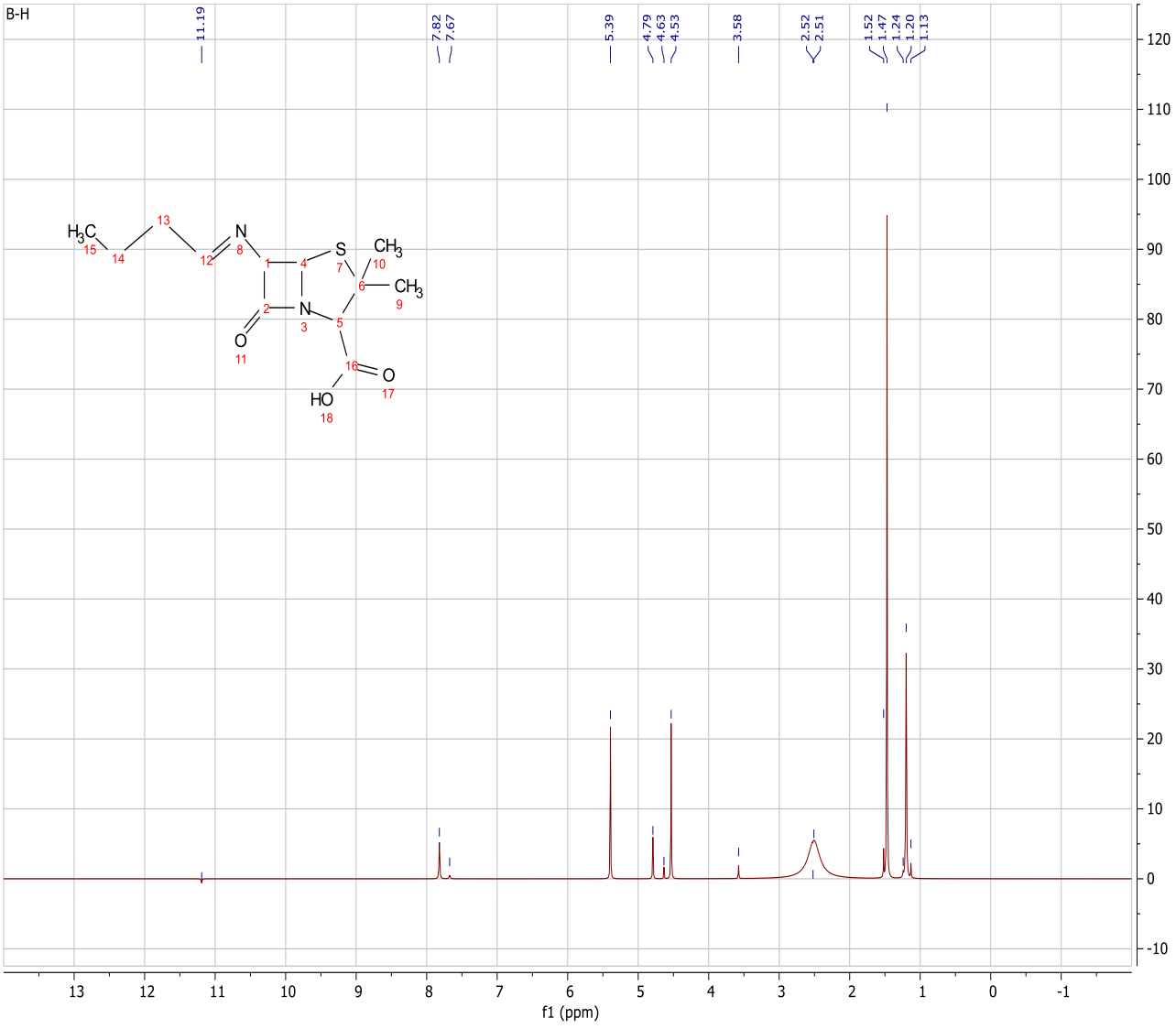


Fig (3.17)^{1}HNMR Spectra of L1

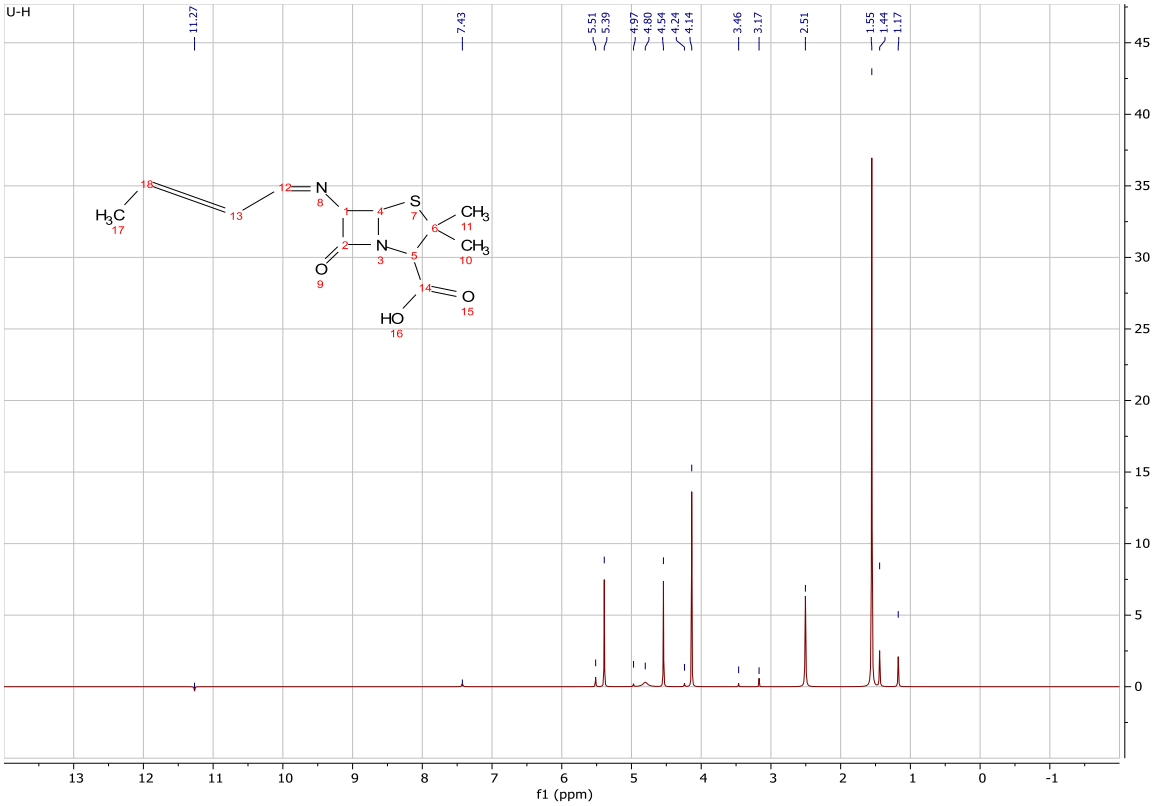


Fig. (3.18) [1]HNMR Spectra of L2

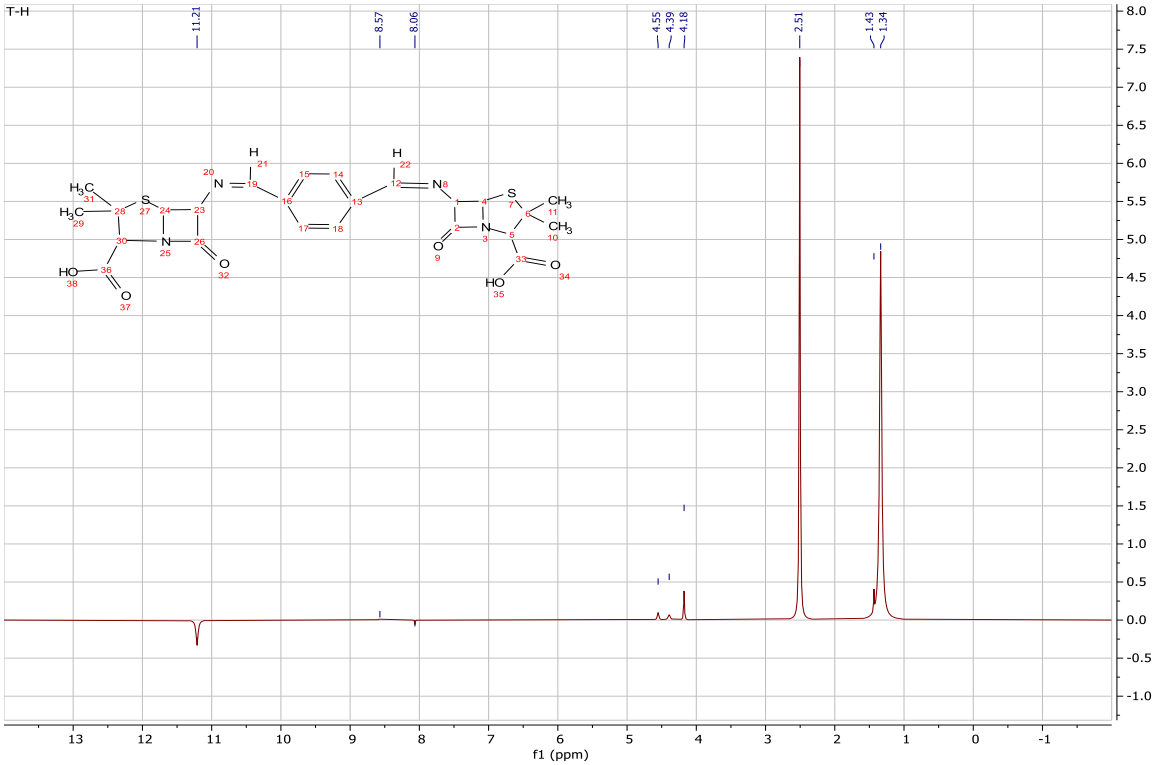


Fig. (3.19) 1HNMR Spectra of L3

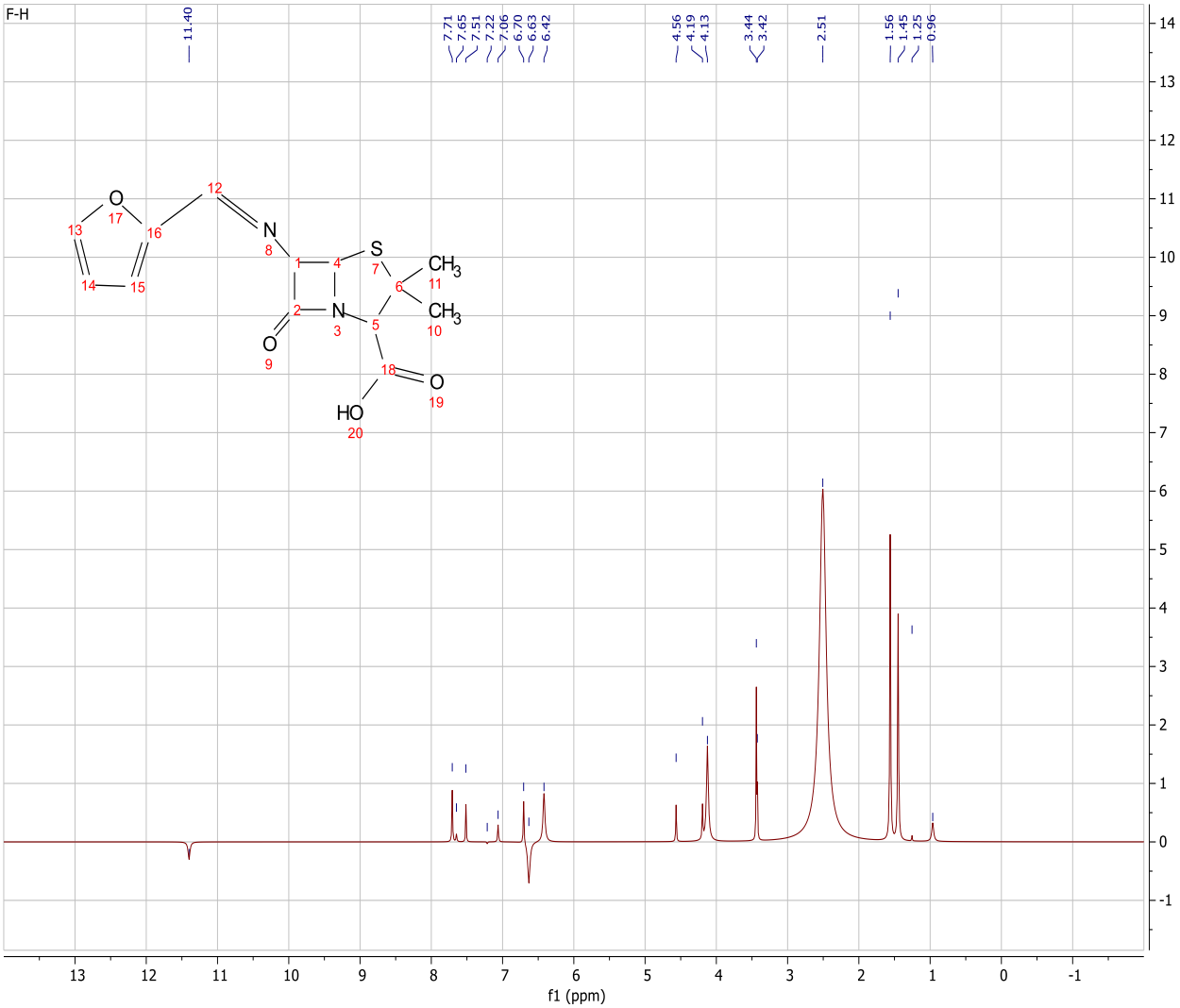


Fig. (3.20)[1]HNMR Spectra of L4

3.9.[13]C-NMR Spectra of the Schiff base Ligands:

The [13]CNMR the ligand's spectrum was recorded DMSO-d[6] solvent was showed a signal at (40 ppm) . Figure below the [13]CNMR spectrum of ligand(L1,L2,L3,L4) showed the azomethine carbon peak at (161,160,167,163) ppm respectively. [M.N. Ibrahim *et.al*., 2011].The (C=O) carboxylic group peak showed at (170,169,171,171)ppm respectively . The carbonyl group peak showed at (173,178,173,175) ppm [Ghufran Kareem Nayyef and Hamid Said,2021]

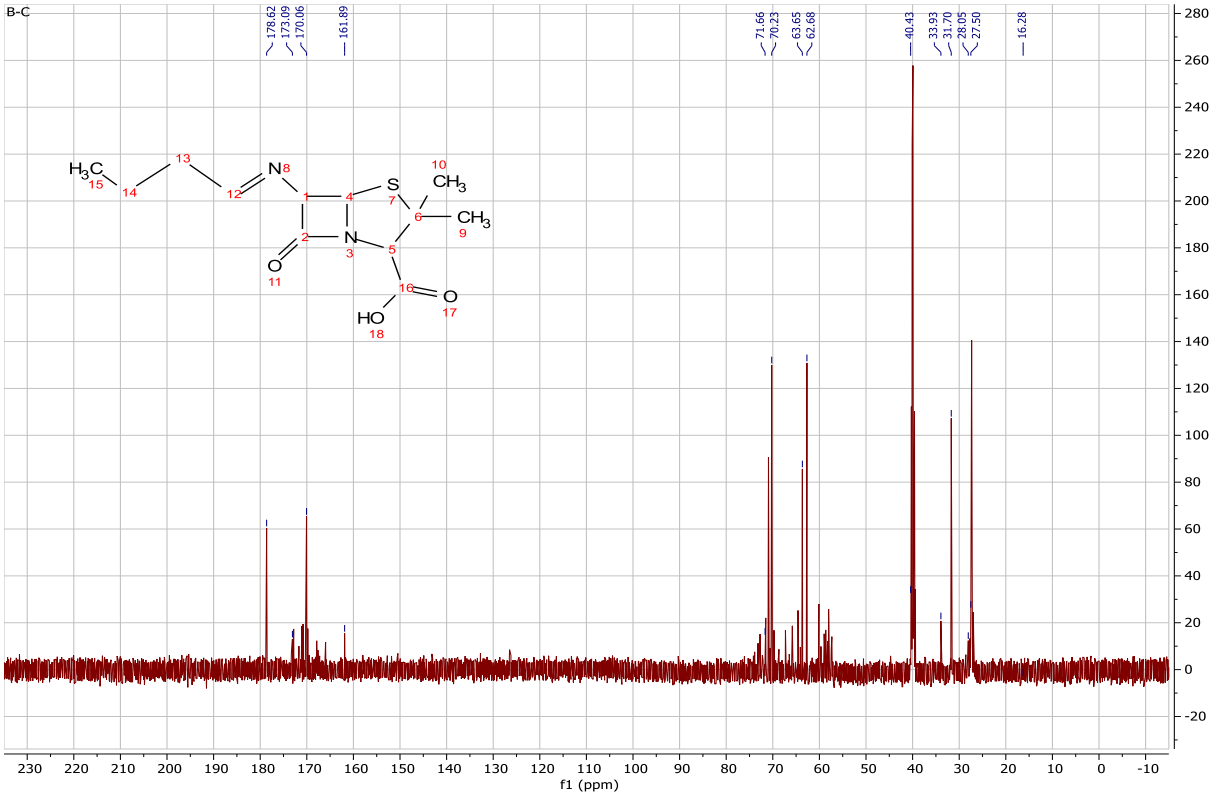


Fig. (3.21) ^{13}CNMR Spectra of L1

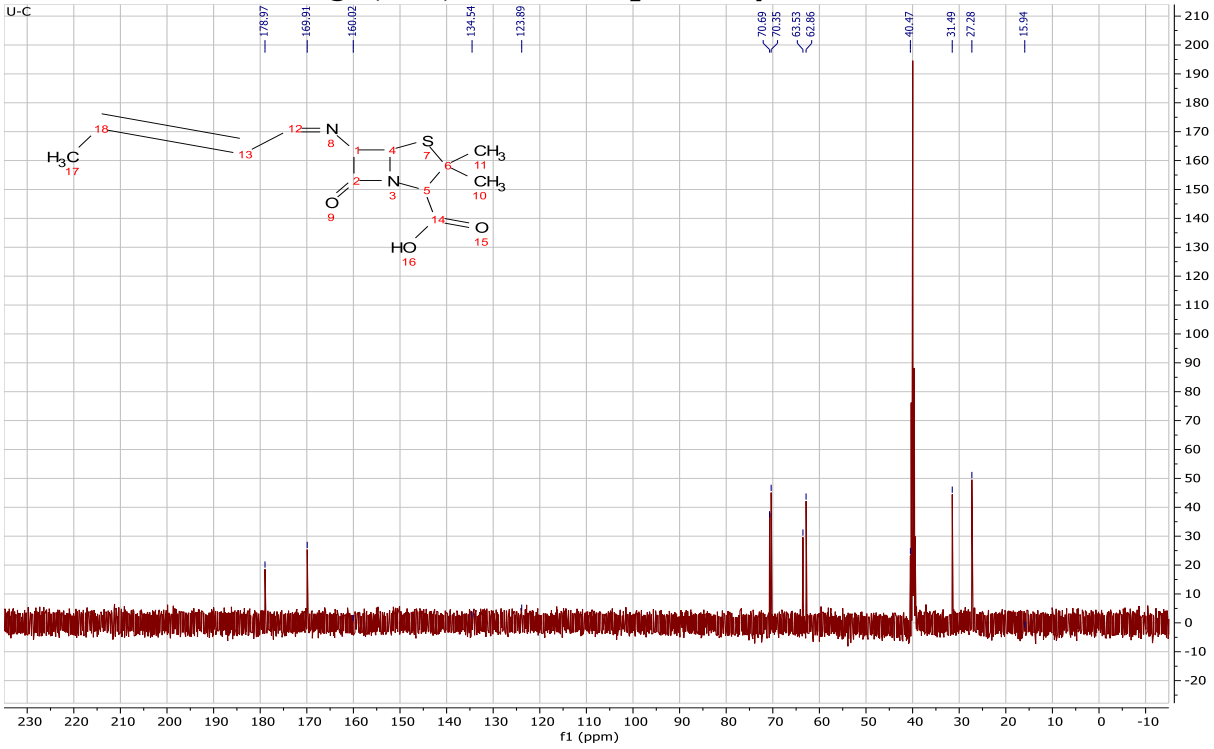


Fig. (3.22)^{13}CNMR Spectra of L2

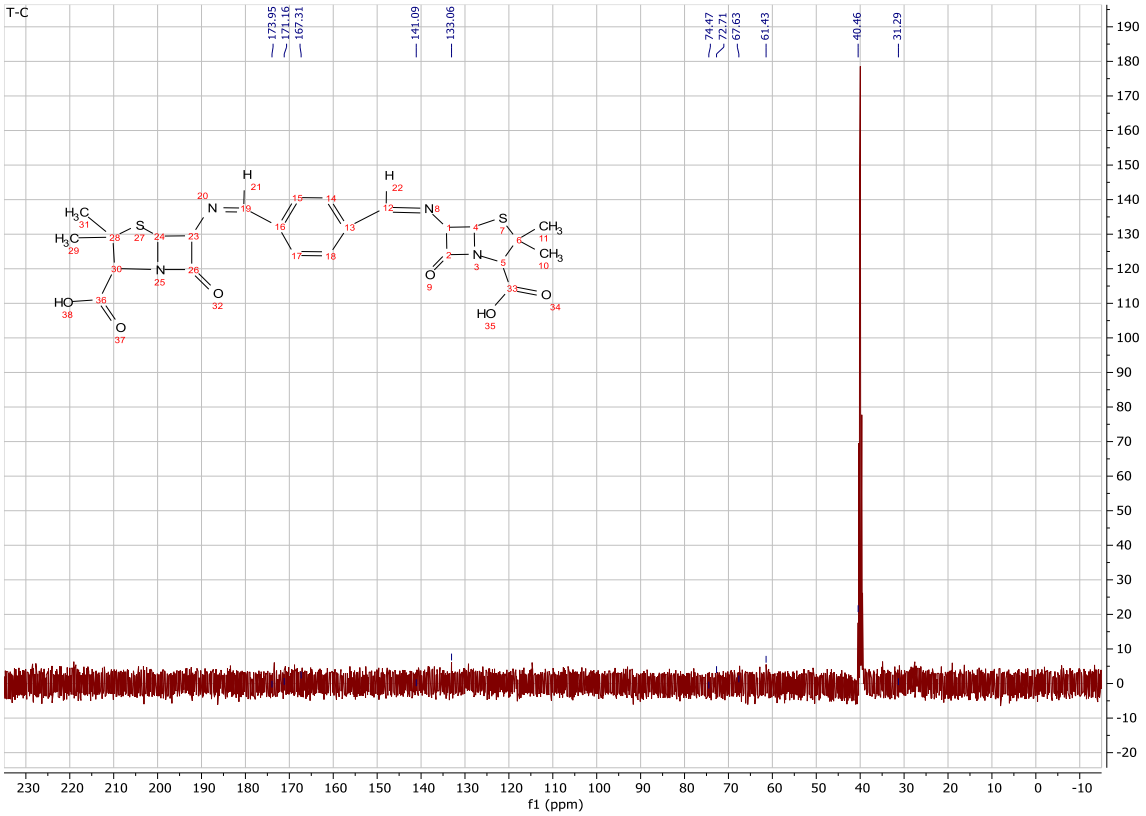


Fig. (3.23) ^{13}CNMR Spectra of L3

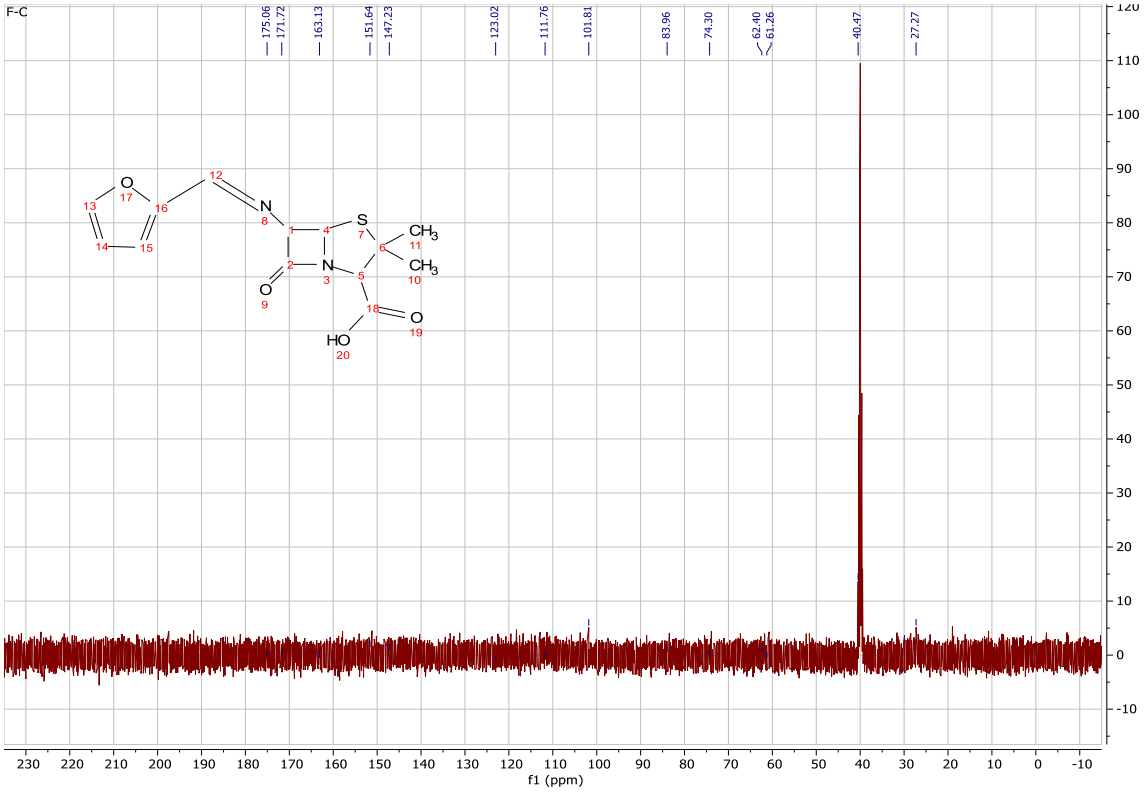


Fig. (3.24)^{13}CNMR Spectra of L4

3.10. U.V-visible absorption the prepared ligands and their complexes:

The electronic spectra of the prepared ligands (L1,L2,L3,L4) were measured in the range(200-400) nm at room temperature using ethanol and DMSO as a solvent. The spectrum of the first the value (L1,L2,L3,L4) (Fig.25,26,27,28) show two absorption bands. The first bands belong to the transitions (π→π*) [Majed, Majid and Majed, 2018],while the second bands refers to the(n→π*). The spectrum of the complexes of ligands (Fig.29,30,31,32) shows also three absorption bands in the range (200-300)nm. The first and the second bands refers to the(π→π*) transition, while the third one is related to the transition(n→π*), which appears due to the presence of a double bond in addition to the presence of heterogeneous atoms in the compound it have ability to grant electronic pair and that confirm the coordination between the metal and the ligand [Haddad, Yousif and Ahmed, 2013].

Table (3.4) Electronic spectra

Compound	Absorption Band ,λ nm	Transfers
L1	**257-349**	**π-π*, n-π***
L2	**273-315**	**π-π*, n-π***
L3	**268-321**	**π-π*, n-π***
L4	**265-311**	**π-π*, n-π***
$[Zn(L_1)_2Cl_2]$	**225-264-312**	**π-π*, π-π*, n-π***
$[Zn(L_2)_2Cl_2]$	**215-268-306**	**π-π*, π-π*, n-π***
$[Zn(L_3)_2Cl_2]$	**217-252-308**	**π-π*, π-π*, n-π***
$[Zn(L_4)_2Cl_2]$	**226-269-309**	**π-π*, π-π*, n-π***

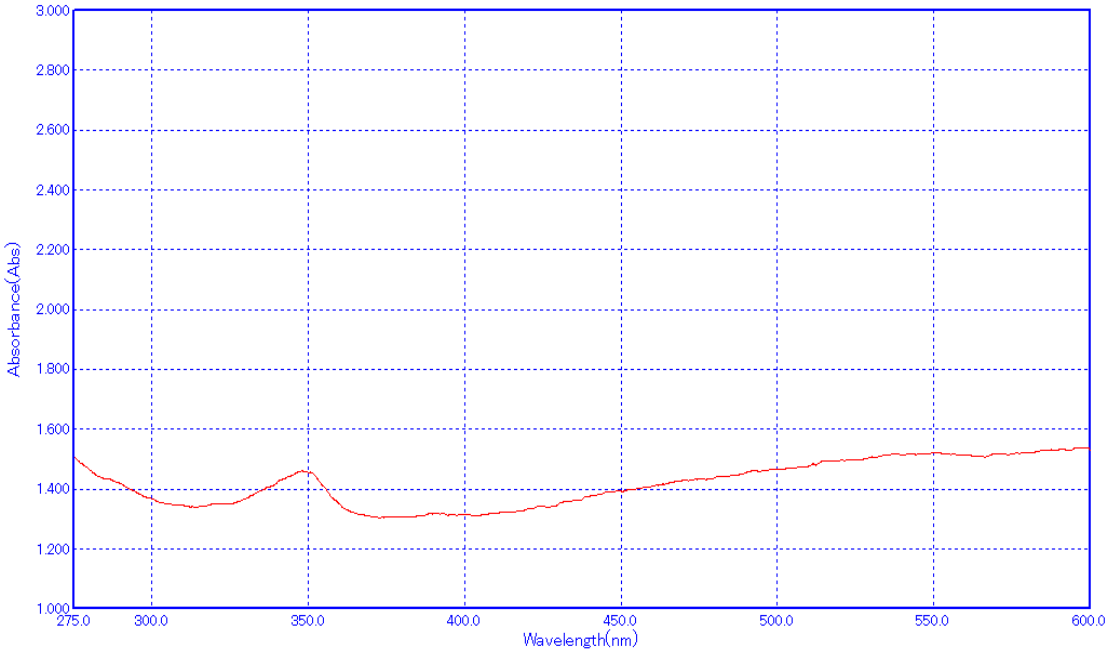


Fig. (3.25) UV-Vis spectrum of [L1]

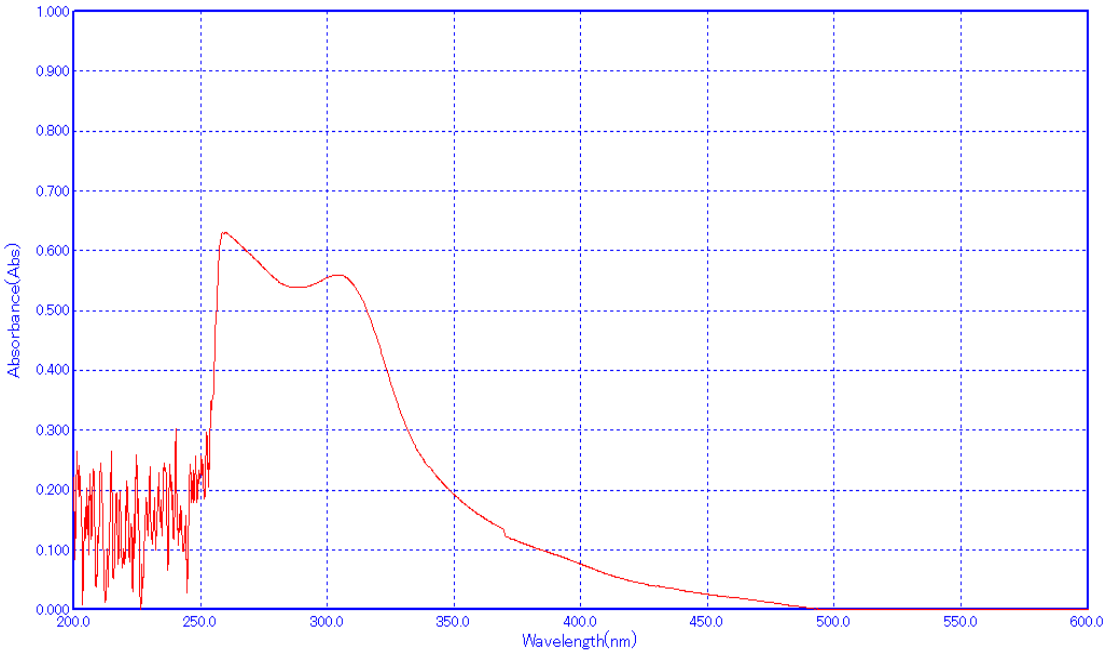


Fig. (3.26) UV-Vis spectrum of [L2]

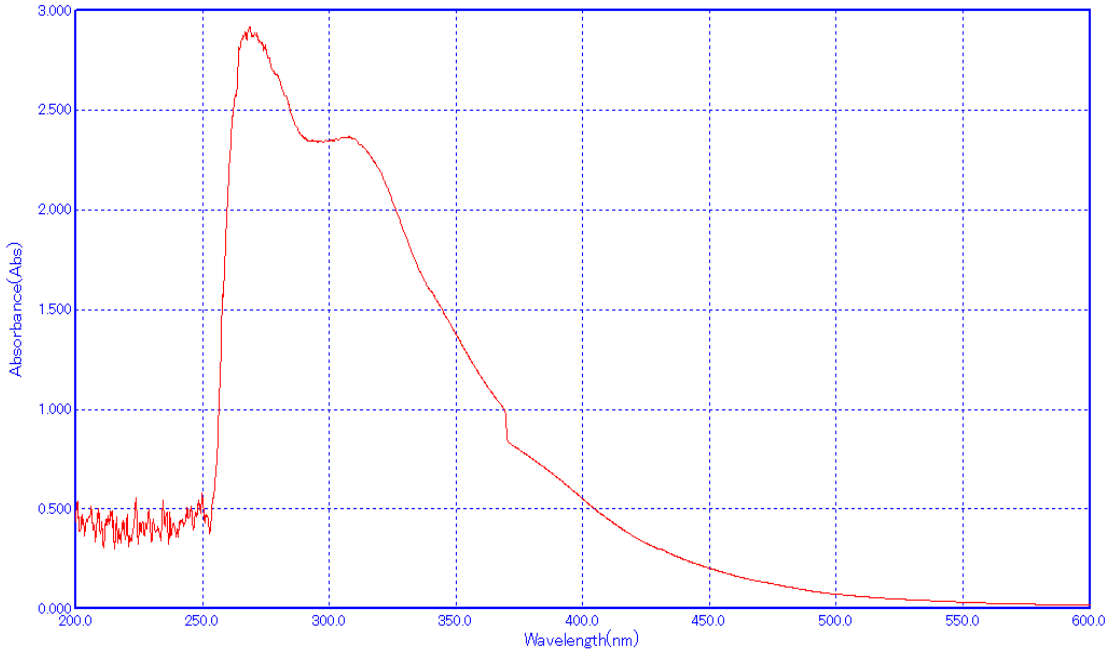


Fig. (3.27) UV-Vis spectrum of [L3]

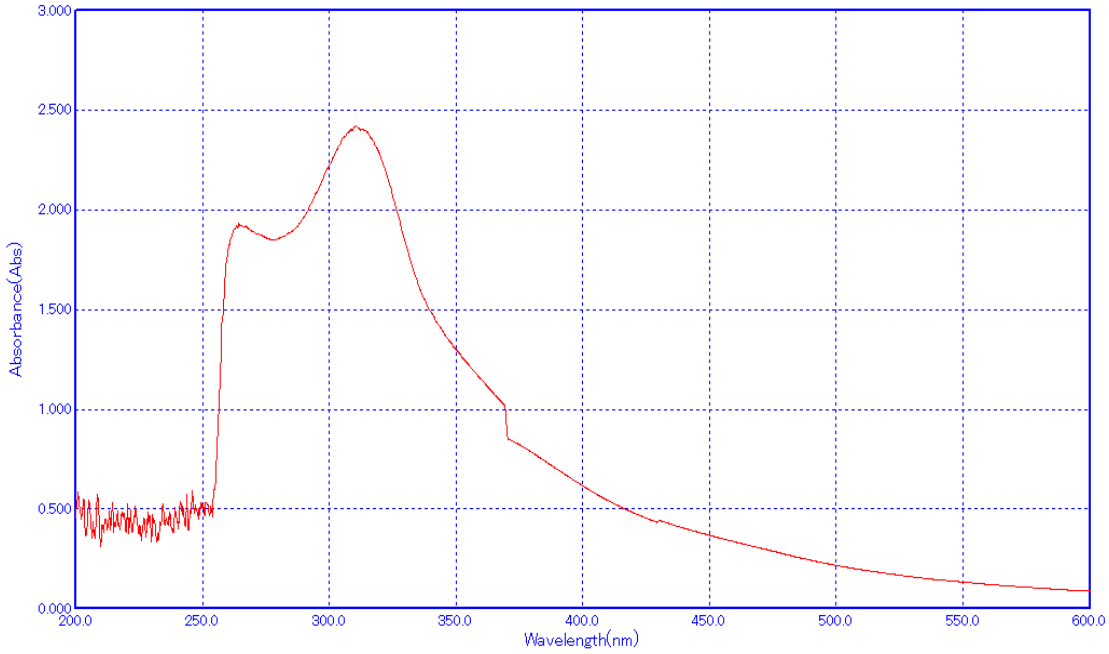


Fig. (3.28) UV-Vis spectrum of [L4]

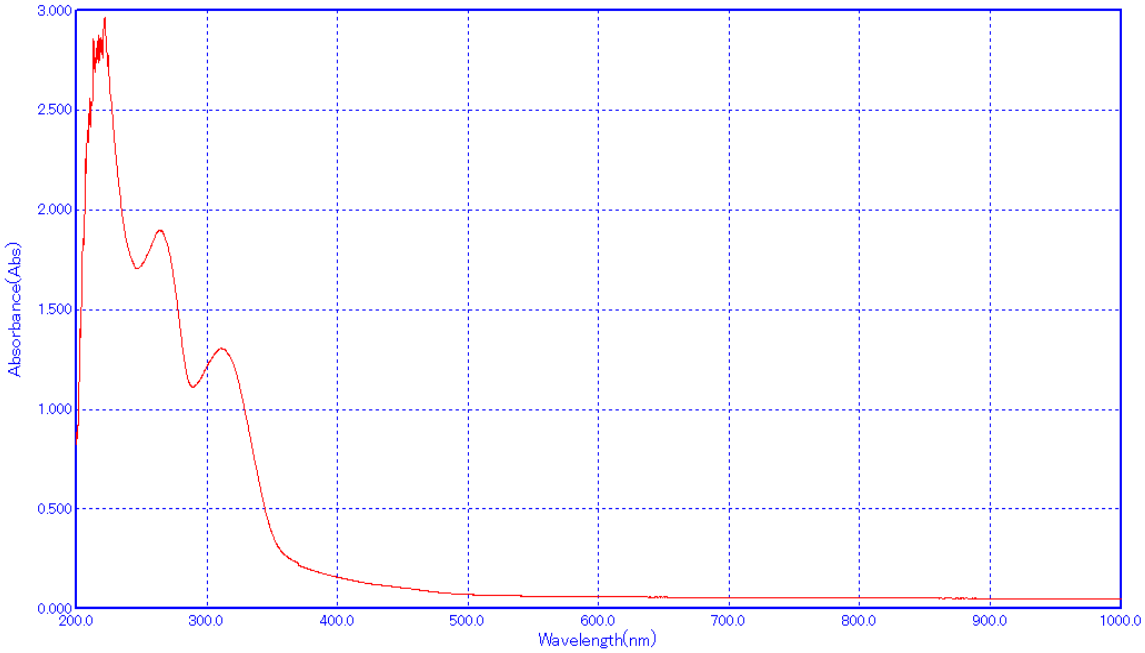


Fig. (3.29) UV-Vis spectrum of [B1]

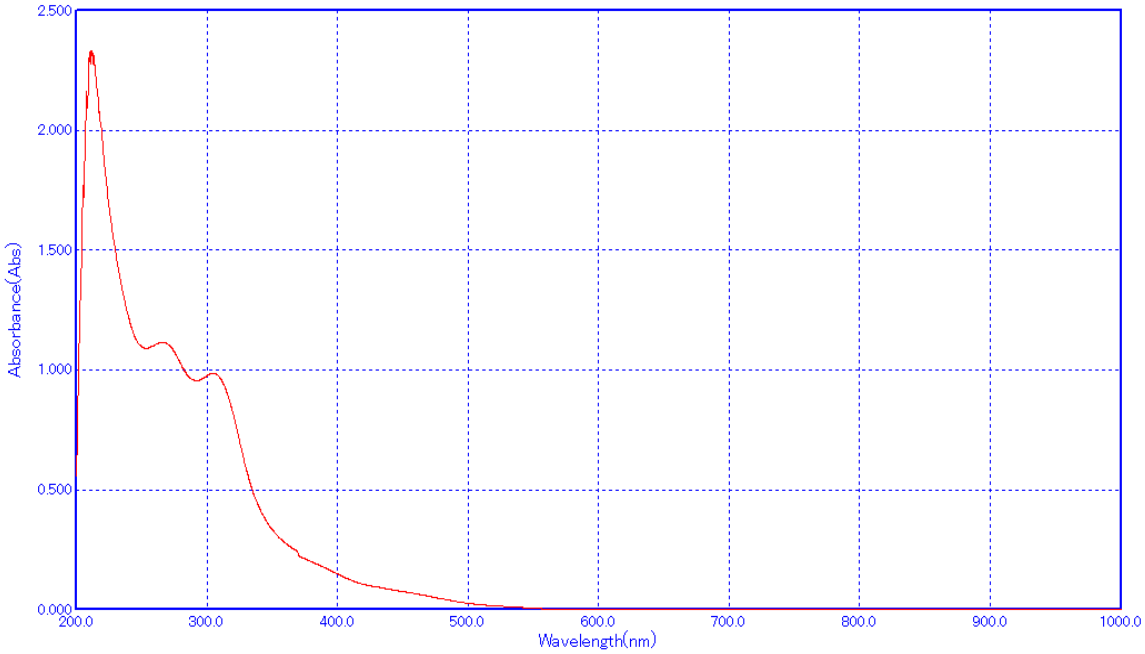


Fig. (3.30) UV-Vis spectrum of [B2]

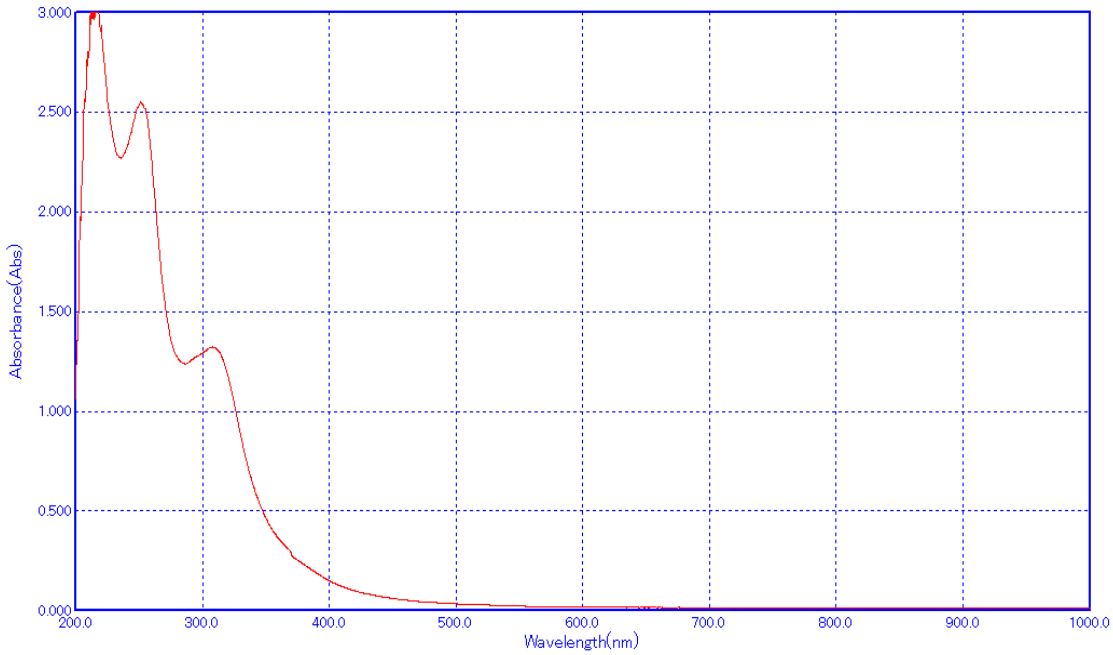


Fig. (3.31) UV-Vis spectrum of [B3]

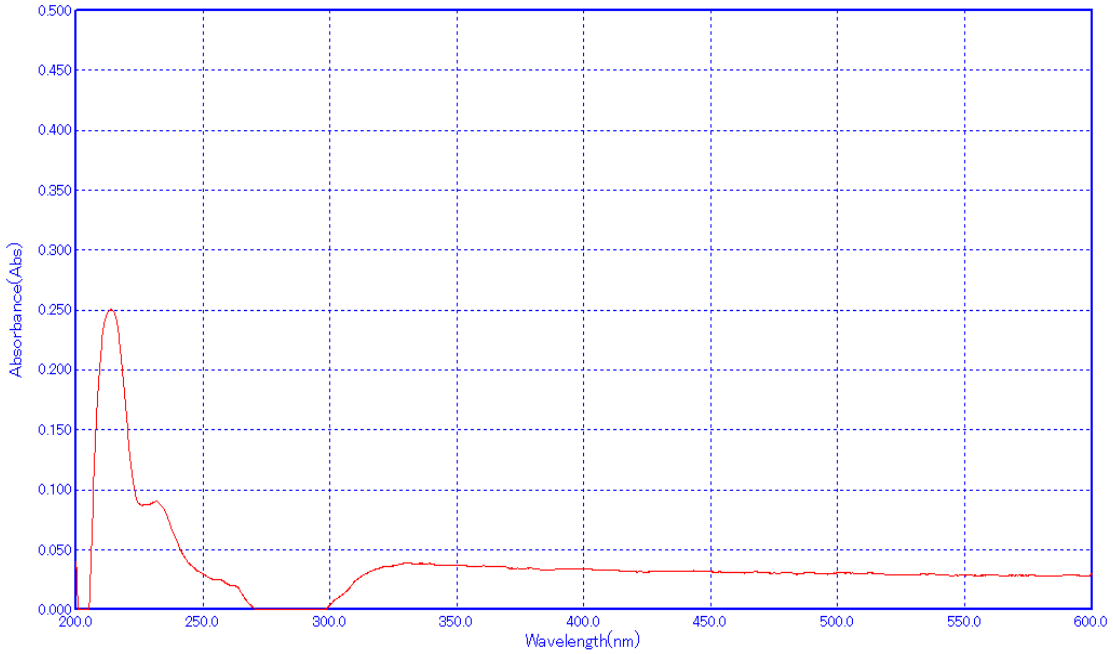


Fig. (3.32) UV-Vis spectrum of [B4]

3.11.Thermal analysis:

TGA experiments were used to investigate the thermal properties of complexes.Fig(33,34,35,36,37) show the TG curves of complexes[Vinusha *et.al.*, 2019]. In Zn(II) complex of (L1,L2,L3,L4), the decomposition takes place in two steps. first steps the complexes showed stability to (194.99,223.51,199.29,204.02)°C respectively indicates the beginning of the decomposition of the organic compound which is attributed to the decomposition of the beta-lactam ring. Second step begins from (265.52,401.82,379.41,501.84)°C of (L1,L2,L3,L4) respectively indicates the end of the decomposition of the organic compound, leaving behind metal oxide as the end product.

Table(3.5) thermal analysis

Complexes	Humidity	Beginning of decomposition °C	End of decomposition °C
B1	**-**	**194.99**	**265.52**
B2	**-**	**223.51**	**401.82**
B3	**64.20**	**199.29**	**379.41**
B4	**-**	**204.02**	**501.84**

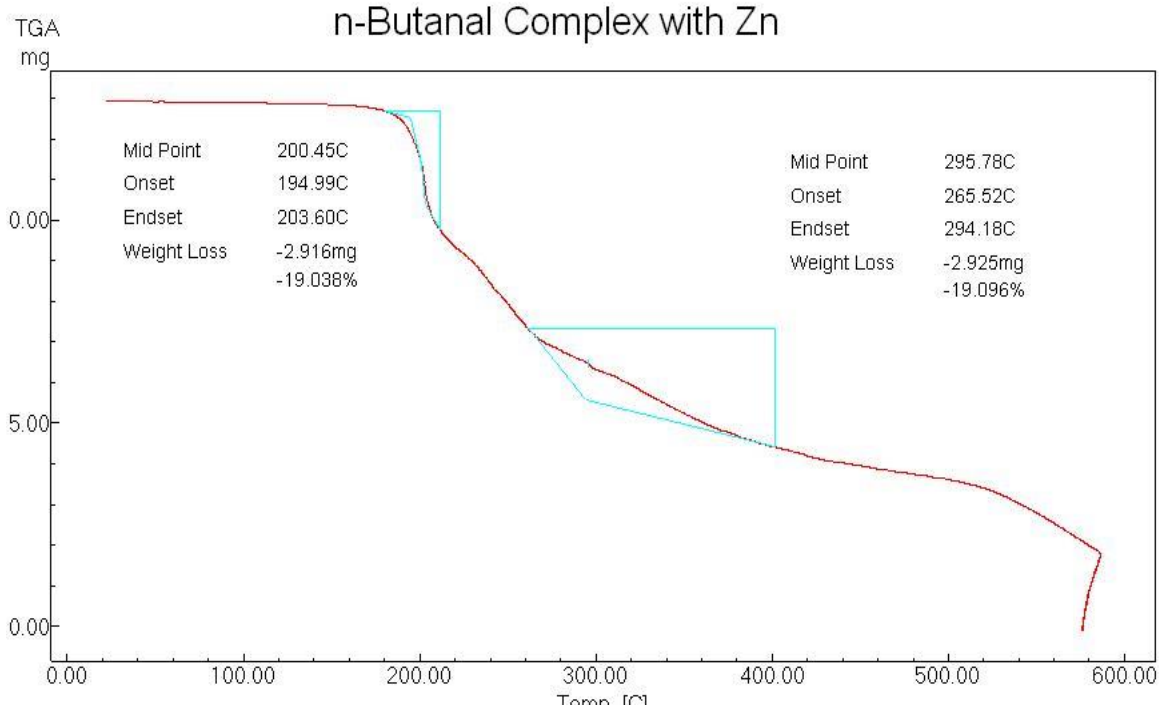


Fig. (3.33)TG curves of B1

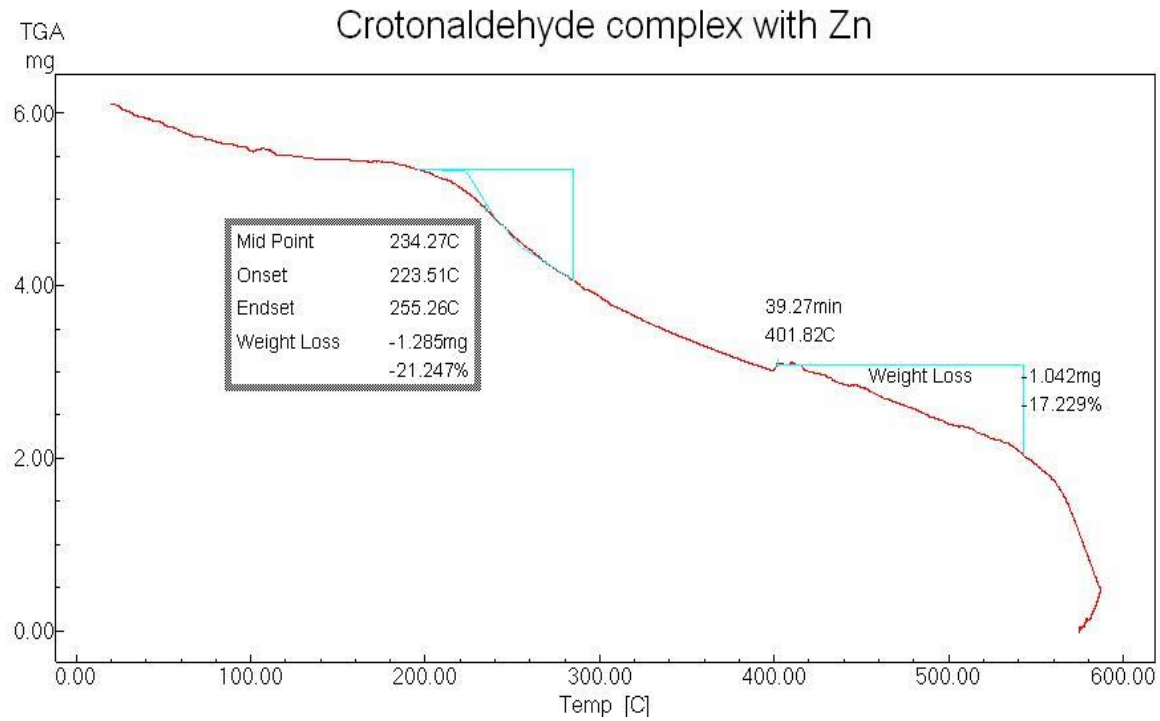


Fig. (3.34)TG curves of B2

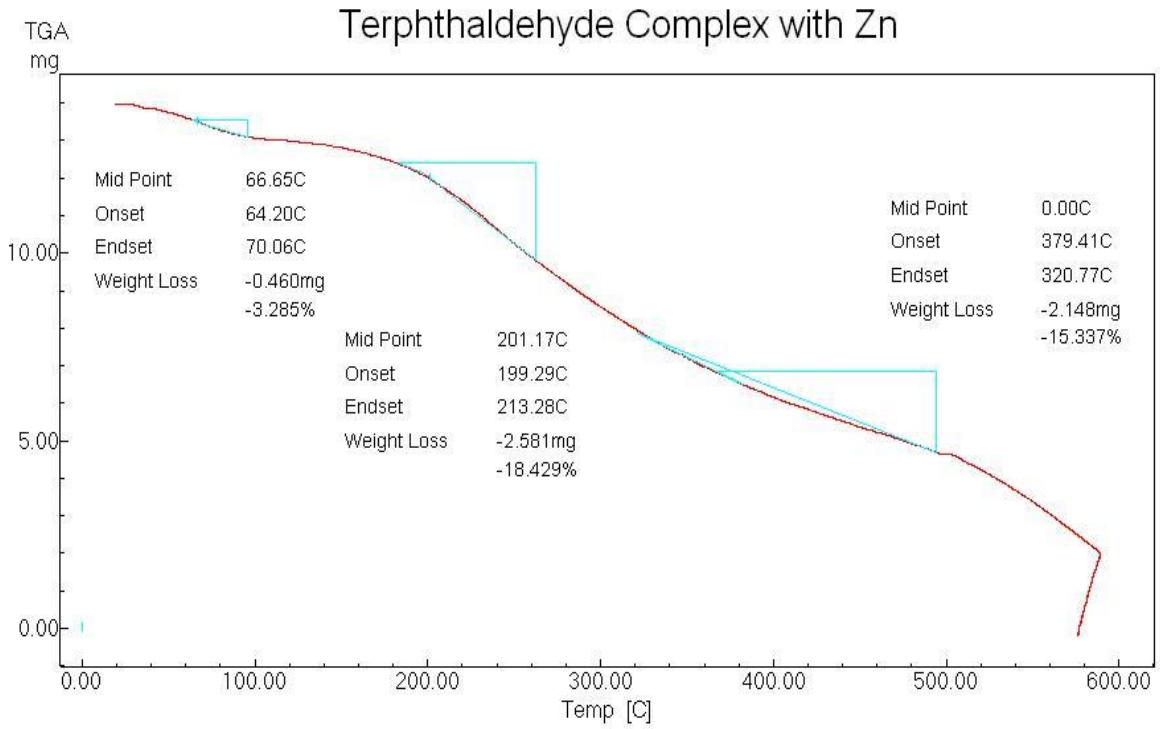


Fig. (3.35)TG curves of B3

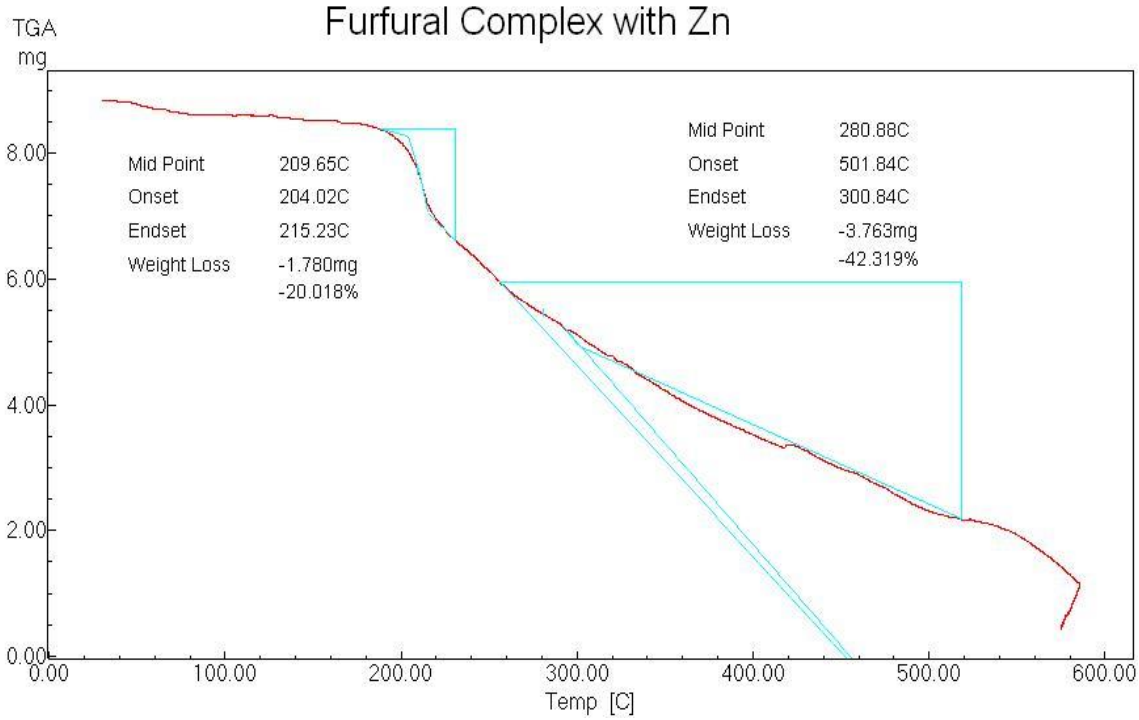


Fig. (3.36)TG curves of B4

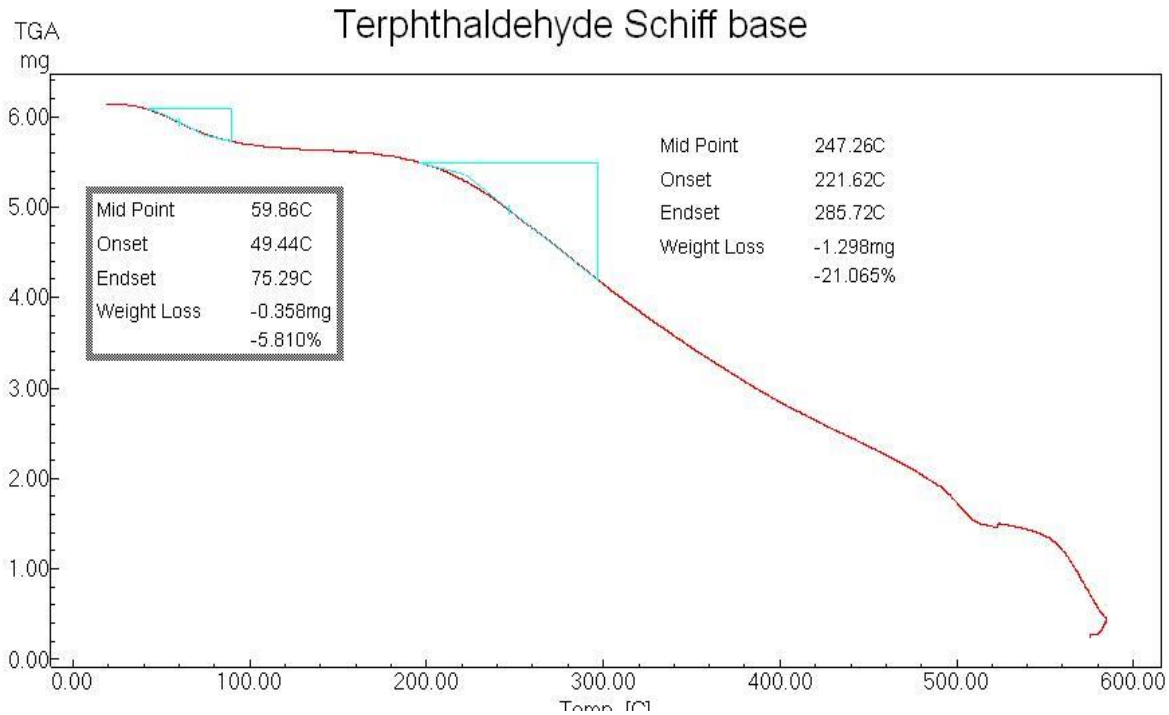


Fig. (3.37)TG curves of L3

3.12.*Atomic absorption:*

The atomic absorption approach was used to calculate the percentage of zinc divalent ions in their complexes. The results reveal a good fit between the theoretical and practical values. In Furthermore, the findings confirm the complexes' hypothesized structure and type hybridization as shown in the table (3.6)

Table (3.6): Practical and theoretical values for the ratio of metals in the prepared complexes and type hybridization

complexes	Theoretical value %	Practical value %	Suggested structure	hybridization
B1	**9.68**	**9.5**	**Octahedral**	**sp^3d^2**
B2	**9.75**	**10.3**	**Octahedral**	**sp^3d^2**
B3	**9.82**	**10.1**	**Octahedral**	**sp^3d^2**
B4	**9.02**	**8.5**	**Octahedral**	**sp^3d^2**

3.13.Molar conductivity

The molar conductivity of solutions is commonly used in coordination chemistry to determine the ionic formulae of compounds in solution, whether neutral or ionic. The higher the conductivity value, the more ions that are liberated in solution[Geary ,1971]. At room temperature, the molar conductance values of the synthesized complexes at a concentration of (10^{-3}M) and dissolved in Dimethyl sulfoxide[DMSO]as a solvent. Were included in the table (3-7). The data shown in this table demonstrated that the conductivity that appeared for complexes was of a non-electrolytic type[Maream *et.al.*,2021].

Table(3.7):The values of molar conductivity of complexes at ($1*10^{-3}$) M in DMSO:

complexes	Molar conductivity ($Ohm^{-1}.mol^{-1}.cm^{-1}$)
$[Zn(L1)_2 Cl_2]$	**21.3**
$[Zn(L2)_2 Cl_2]$	**19.2**
$[Zn(L3) Cl_2]$	**20.1**
$[Zn(L4)_2 Cl_2]$	**22.2**

3.2. oxazepine

Recently, the cycloaddition process to synthesize the 1,3-oxazepine ring,this sort of reaction is not restricted and produces a variety of 1,3-oxazepine ring derivatives, The kind of the cycloaddition procedure employed in the production of the 1,3-oxazepine ring was designated as (2+5)= 7,cycloaddition process in which two imine atoms were added as two-membered components to a five-membered component, such as maleic or phthalic anhydrides, to yield a seven-membered anhydride

heterocycle [Hassan Abood, 2010]The intriguing biological activities drew our attention to the chemistry of nitrogen, oxygen heterocyclic. Some of the synthesized compounds were tested in vitro for antibacterial activity against various bacterial strains (*E.coli, pseudomonas*) [Al-Janaby and Al-Jobory, 2014].Oxazepine derived was introduced at this period for use in mental relaxation characterized by worry and tension[Sa'adi Hassan and Hame, 2019].The relevance of 1,3-oxazepine is attributed to its uses as an anticonvulsant, depressive, skeletal muscle relaxant, neuroleptic, anticancer agent, antimicrobial, anti-corrosion, and anti-anxiety medication[Kshash and Mokhlef, 2017].

3.14 Solubility and Physical properties of compound:

Using various solvents, the solubility of the obtained as derivatives oxazepine and its complexes formed by transitional metal ion [Zn(II)] was investigated. The results in Table (3.8) demonstrated that the a oxazepine nd all of their complexes are insoluble in water. They are also weakly soluble in a wide range of organic solvents, including methanol, ethanol, Hexane ,and with the exception of DMSO. As the table below shows Melting point, Yield ,and Colors both ligands and their complexes.

Table 3.8. Physical properties of the synthesized compounds

Compd.	M.P (C°)	Color	Yield (%)	Solubility				
				H_2O	C_2H_6O	DMSO	CH_3OH	C_6H_6
C_1	190-194	Light yellow	67%	–	δ	+	δ	δ
C_2	201-205	Pale yellow	64%	–	δ	+	δ	δ
C_3	183-186	Yellow	63%	–	δ	+	δ	δ

C_4	142-145	Orange	80%	_	δ	+	δ	δ
C_5	149-153	Light nutty	87%	_	δ	+	δ	δ
C_6	128-130	Nutty	85%	_	δ	+	δ	δ
C_7	163-165	Gray	81%	_	δ	+	δ	δ
C_8	171-176	Gray	79%	_	δ	+	δ	δ
C_9	158-160	Gray	85%	_	δ	+	δ	δ
D_1	255-259	Off white	62%	_	δ	+	δ	δ
D_2	241-244	light beige	74%	_	δ	+	δ	δ
D_3	232-235	Pale yellow	68%	_	δ	+	δ	δ
D_4	210-215	Light orange	78%	_	δ	+	δ	δ
D_5	241-244	Orange	84%	_	δ	+	δ	δ
D_6	201-204	Light nutty	88%	_	δ	+	δ	δ
D_7	230-232	Gray	84%	_	δ	+	δ	δ

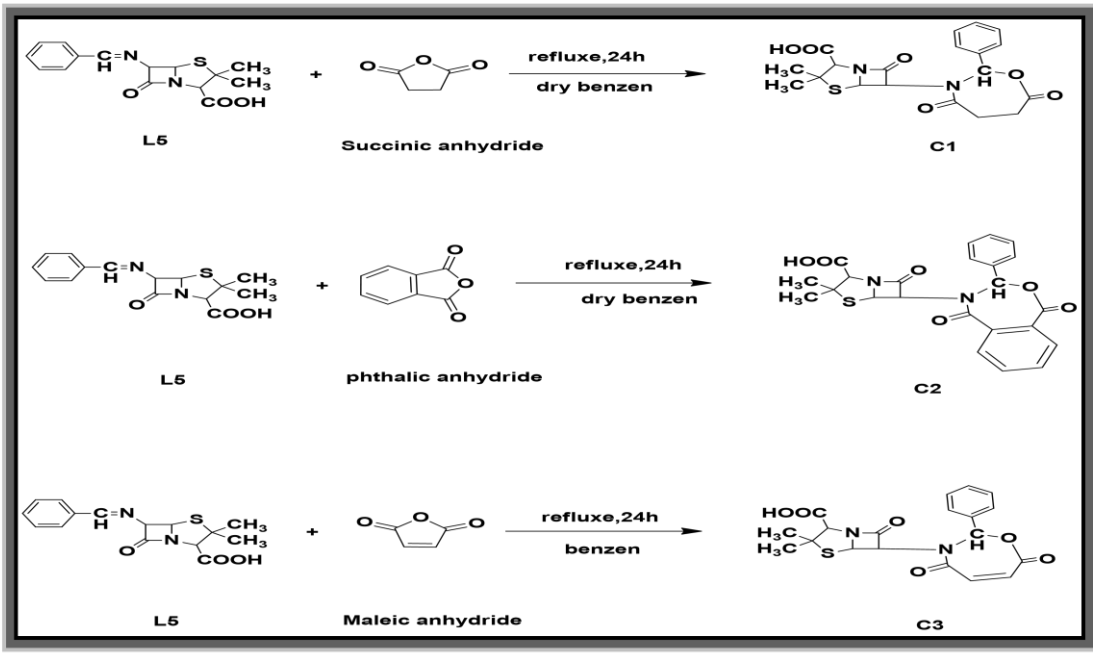
D_8	**232-236**	**Light gray**	**86%**	**_**	**δ**	**+**	**δ**	**δ**
D_9	**229-236**	**Very light gray**	**90%**	**_**	**δ**	**+**	**δ**	**δ**

δ partial soluble

3.15.Synthesis of oxazepine's :

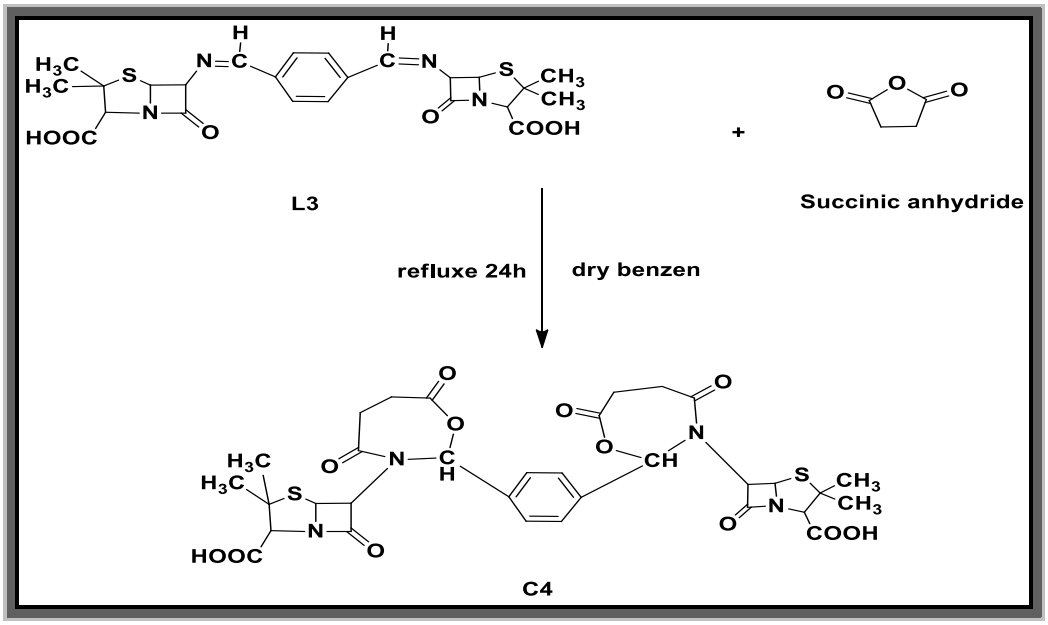
The reaction of maleic anhydride, succinic anhydride, and phthalic anhydride with azomethines (L3, L4 ,L5), which are previously prepared in order to produce the seven-membered cyclic ring, yielded derivatives of 1,3-oxazepine (C1,C2,C3,C4,C5,C6,C7,C8,C9) [Ahmed *et al.*, 2018]. All of the 1,3-oxazepine synthesized, FT-IR, ^{1}H NMR, and ^{13}C NMR spectroscopy were used to identify the compounds.

3.15.1.(L5) with succinic anhydride, phthalic anhydride and maleic anhydride respectively:

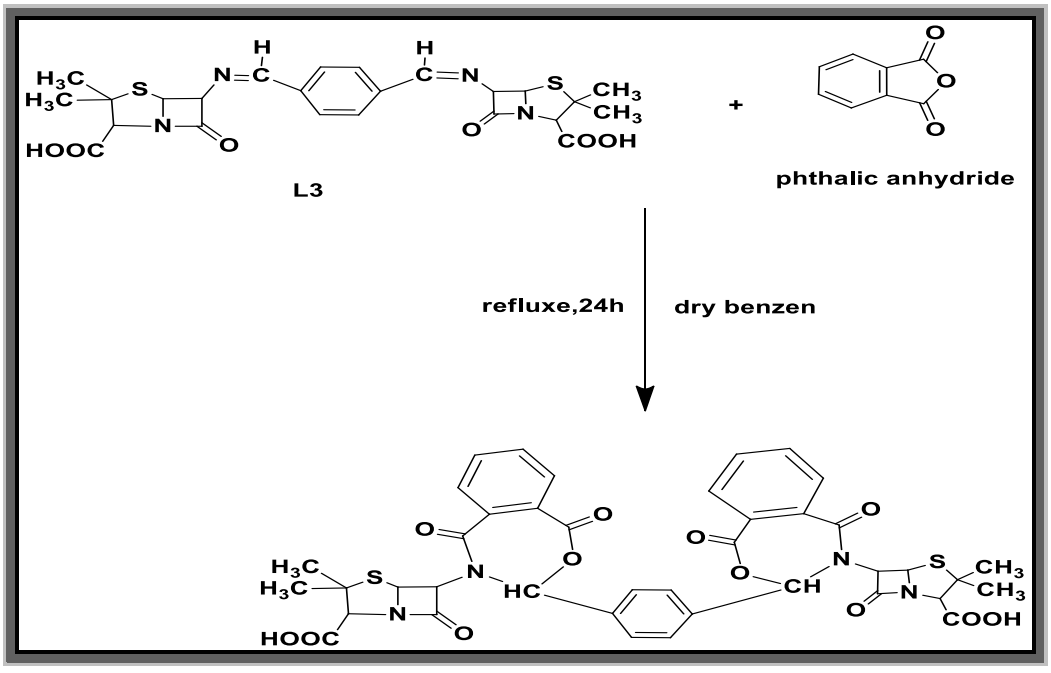


Eq (3.6) composition equation (C, C2, C3)

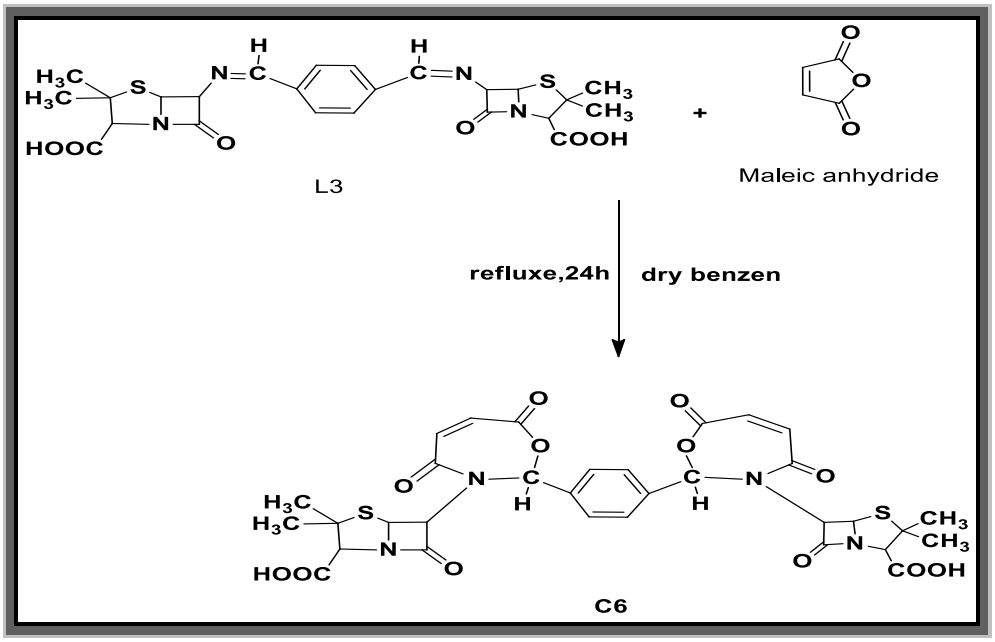
3.15.2.(L3) with succinic anhydride, phthalic anhydride and maleic anhydride respectively:



Eq (3.7) composition equation(C4)

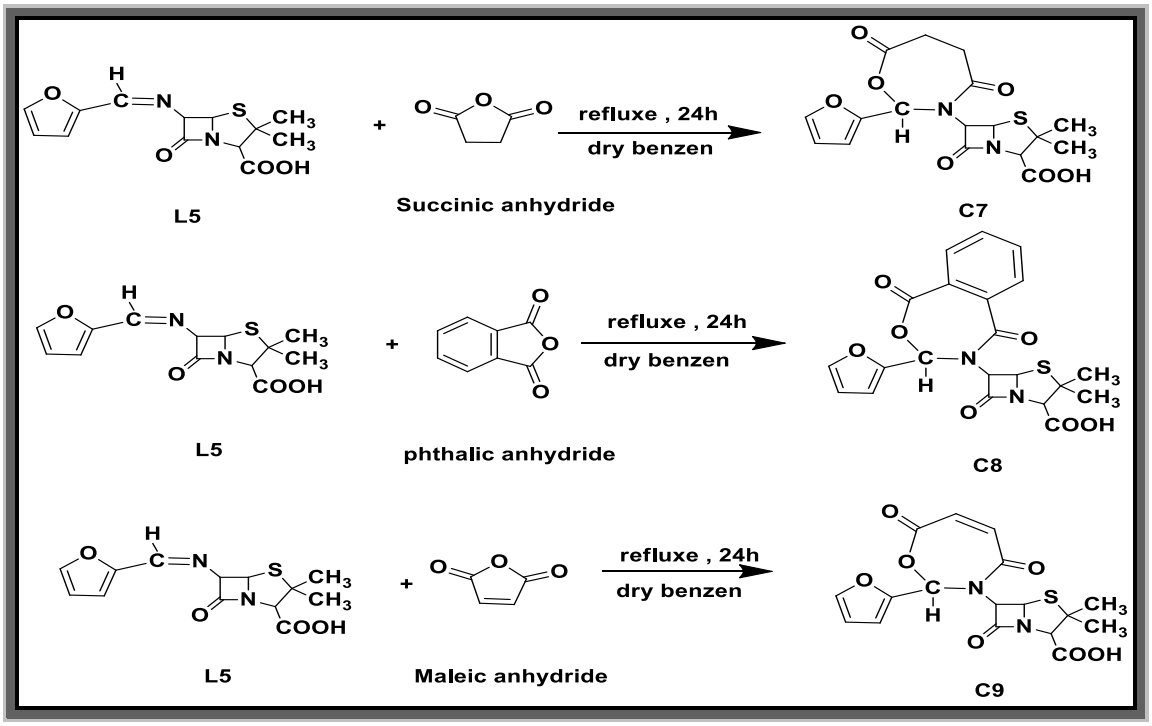


Eq (3.8) composition equation(C5)



Eq (3.9) composition equation(C6)

3.15.3.(L4) with succinic anhydride, phthalic anhydride and maleic anhydride respectively:



Eq (3.10) composition equation (C7, C8, C9)

3.16. Synthesis of oxazepine's complexes:

The reflux reaction was used to create all of the metal complexes The structure of the complexes is shown in figure below and demonstrates that the prepared 1,3- oxazepine's (C1,C2,C3,C7,C8,C9) are Bidentate chelating. and the preparation ratio for all complexes is 1:2, [metal: ligand] ,except for (C4,C5,C6) complex, which is 1:1, [metal: ligand].

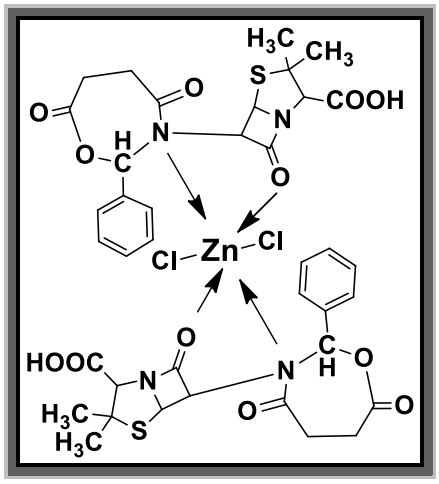


Fig (3.38): D1

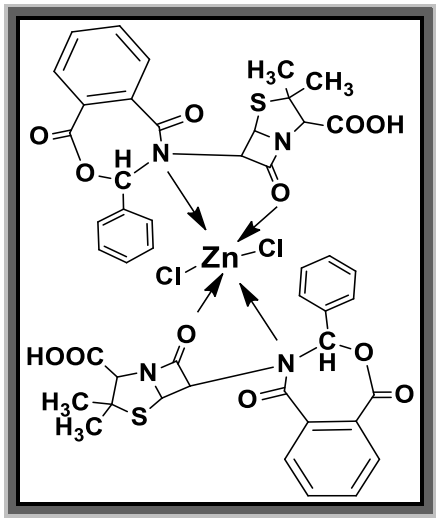


Fig (3.39): D2

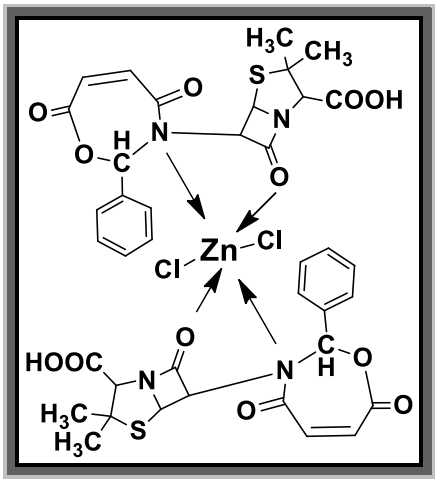


Fig (3.40): D3

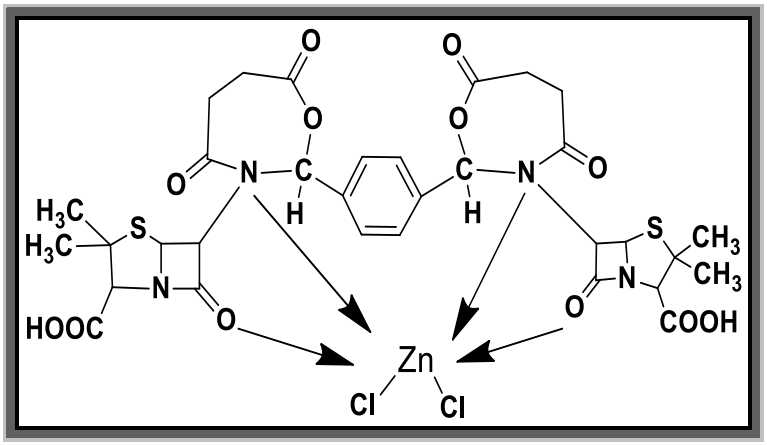


Fig (3.41): D4

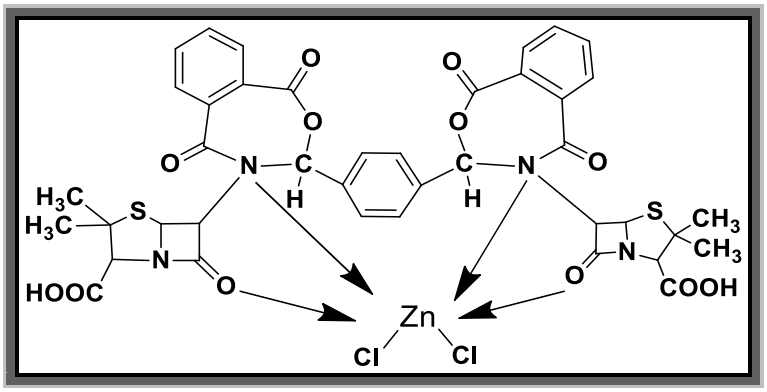


Fig (3.42): D5

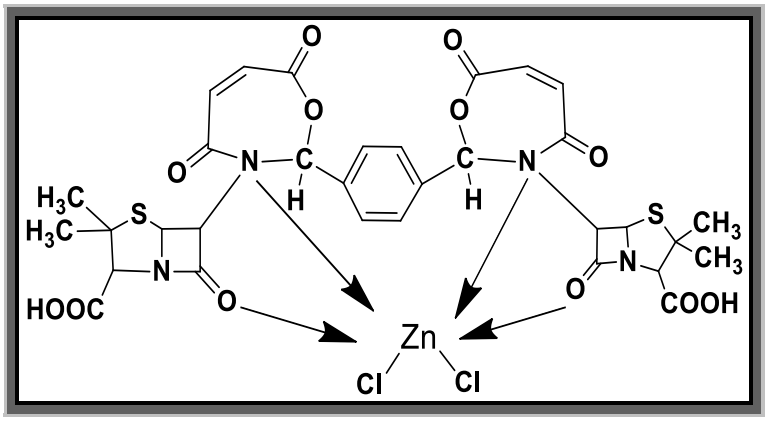


Fig (3.43): D6

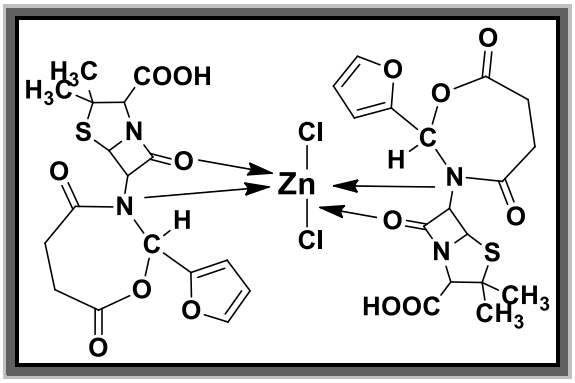


Fig (3.44): D7

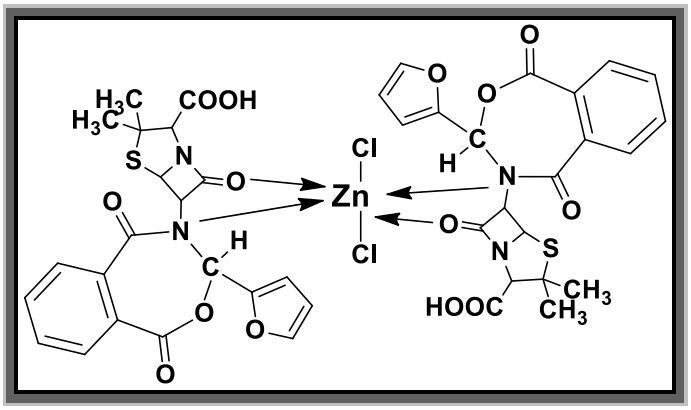


Fig (3.45): D8

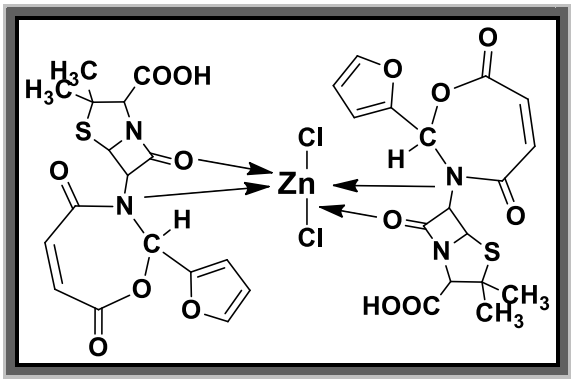


Fig (3.46): D9

3.17. FT-IR Spectra of oxazepine's (C1, C2, C3, C4, C5, C6, C7, C8, C9):

The FT-IR spectra of disubstituted 1,3-oxazepine compound derivatives revealed the absence of the stretching absorption bands of the azomethine group (C=N) , Indication of the formation of (1,3) oxazapine compounds [Ayfan, Muslim and Noori, 2019].The strong and broad absorption band at (3350-4550) cm^{-1} attributed to the υ(O-H) of and carboxylic [Hassan Abood, 2010].The absorption band at (3000-3200) cm^{-1} attributed to the υ(C-H) Aromatic[Abid, Tawfeeq and Muslim, 2017].The absorption band at (1600-1700) cm^{-1} attributed to the υ(C=O) Lactone[Sa'adi Hassan and Hame,2019]and the band at(1700-1750)cm^{-1} attributed to the υ(C=O) Lactam[Khudhair, Abbas and Jber ,2020].

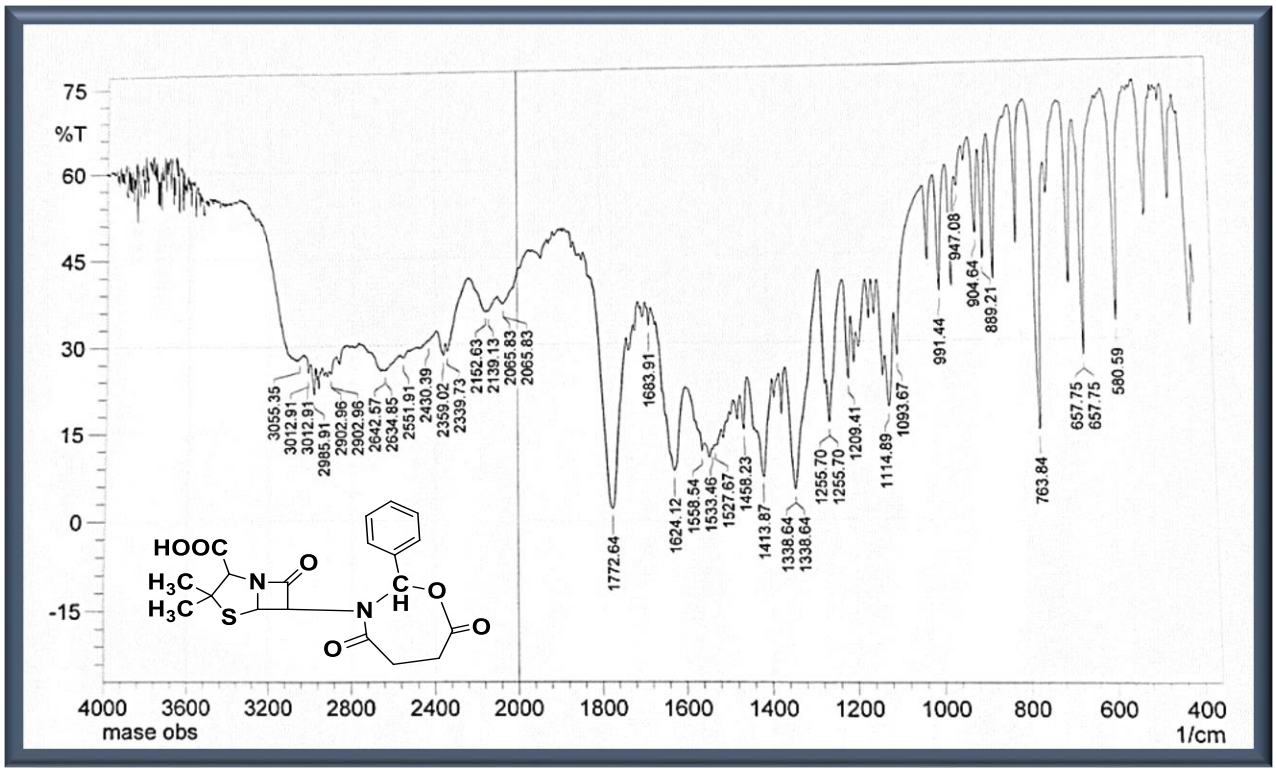


Fig (3-47): FTIR spectrum for (C1)

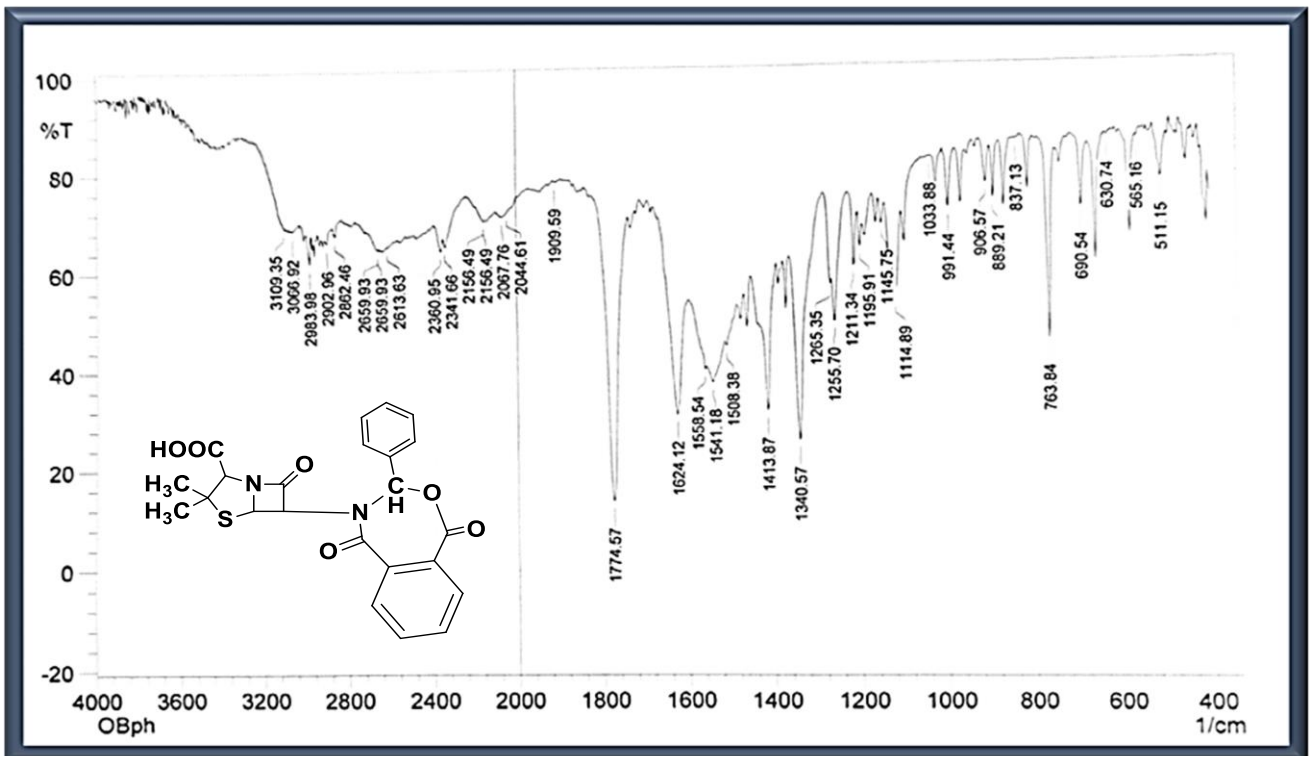


Fig (3-48): FTIR spectrum for (C2)

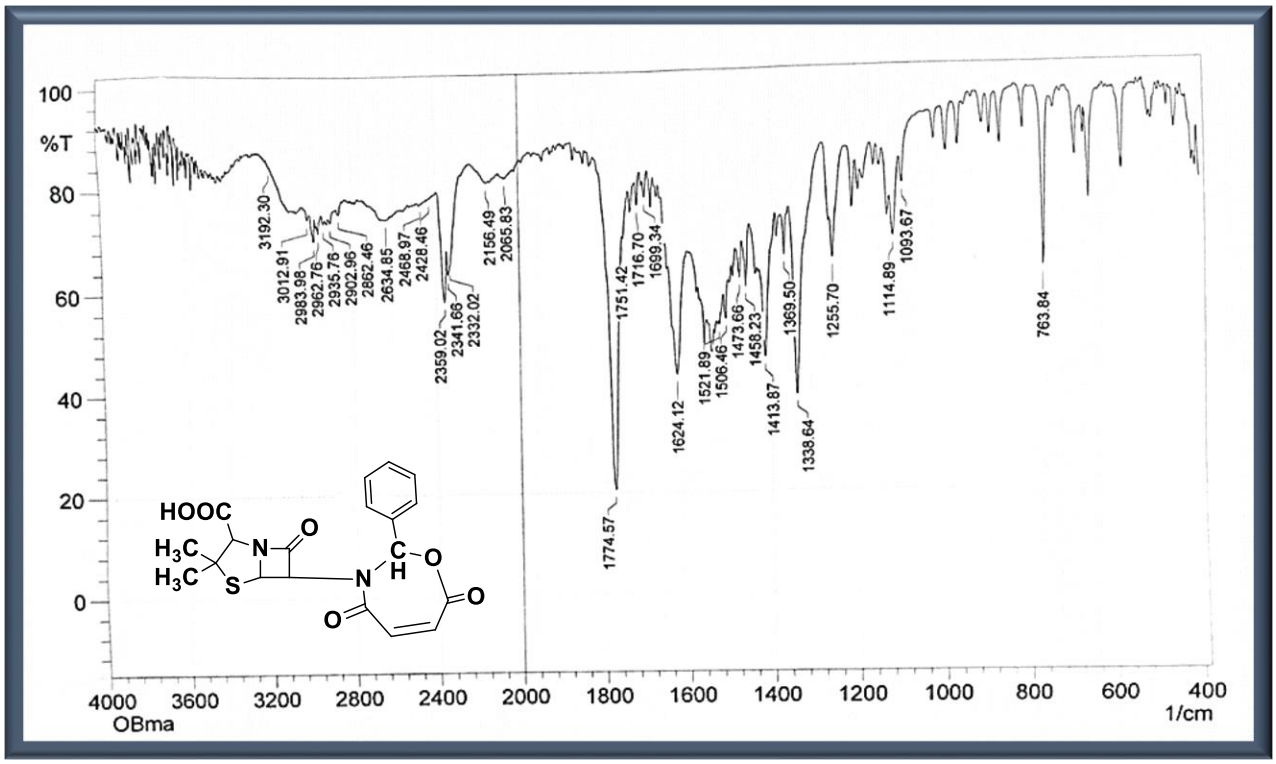


Fig (3-49): FTIR spectrum for (C3)

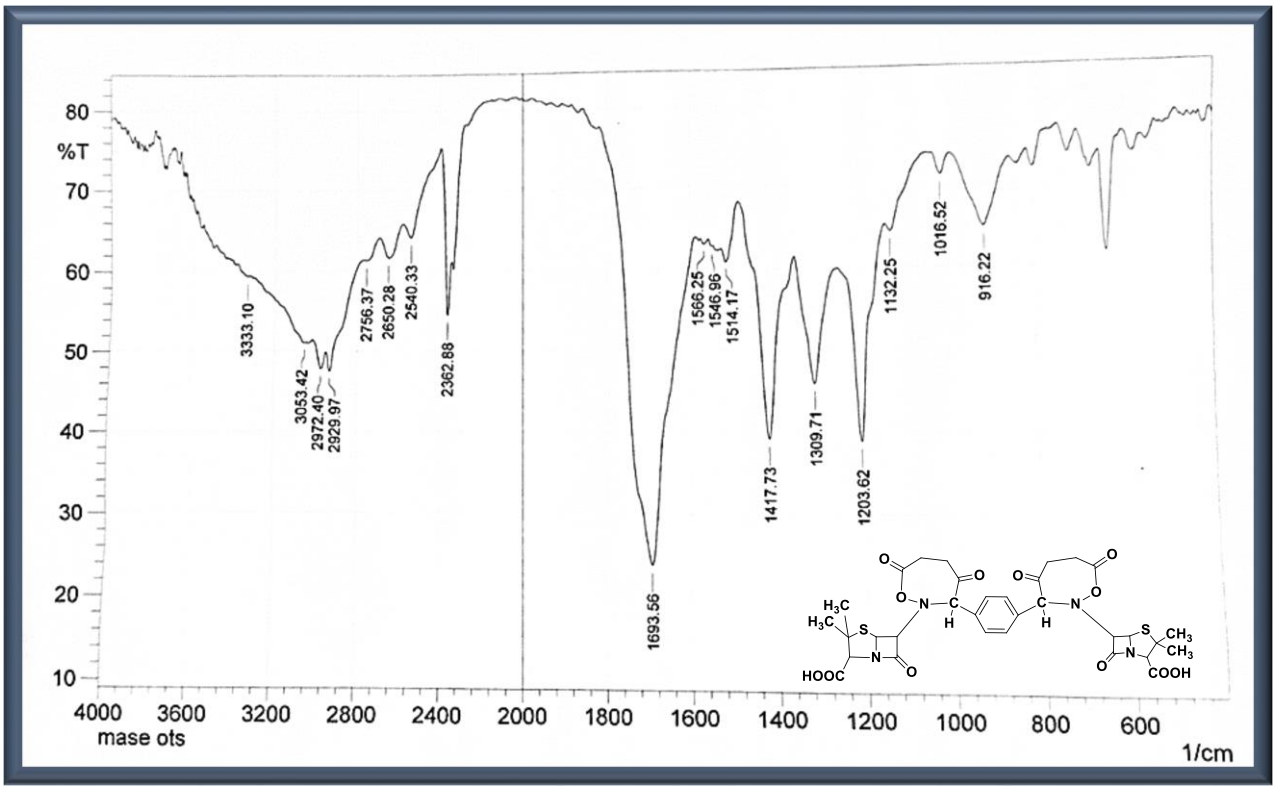


Fig (3-50): FTIR spectrum for (C4)

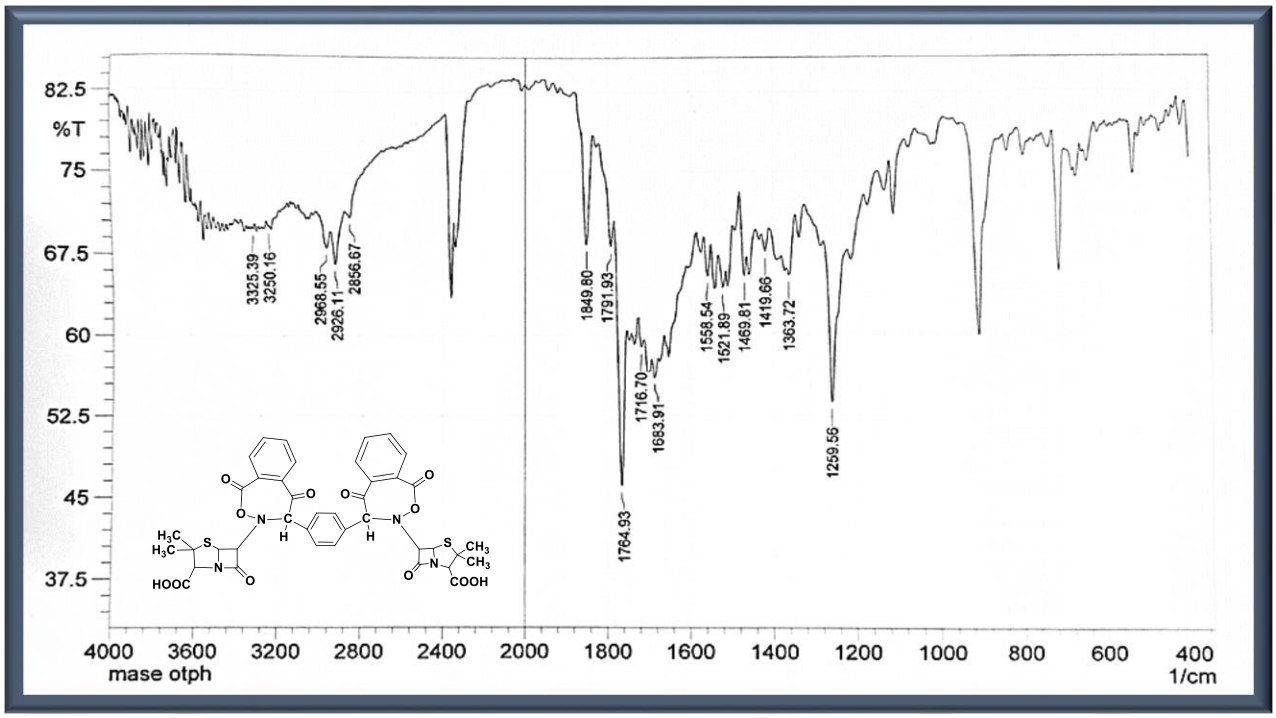


Fig (3-51): FTIR spectrum for (C5)

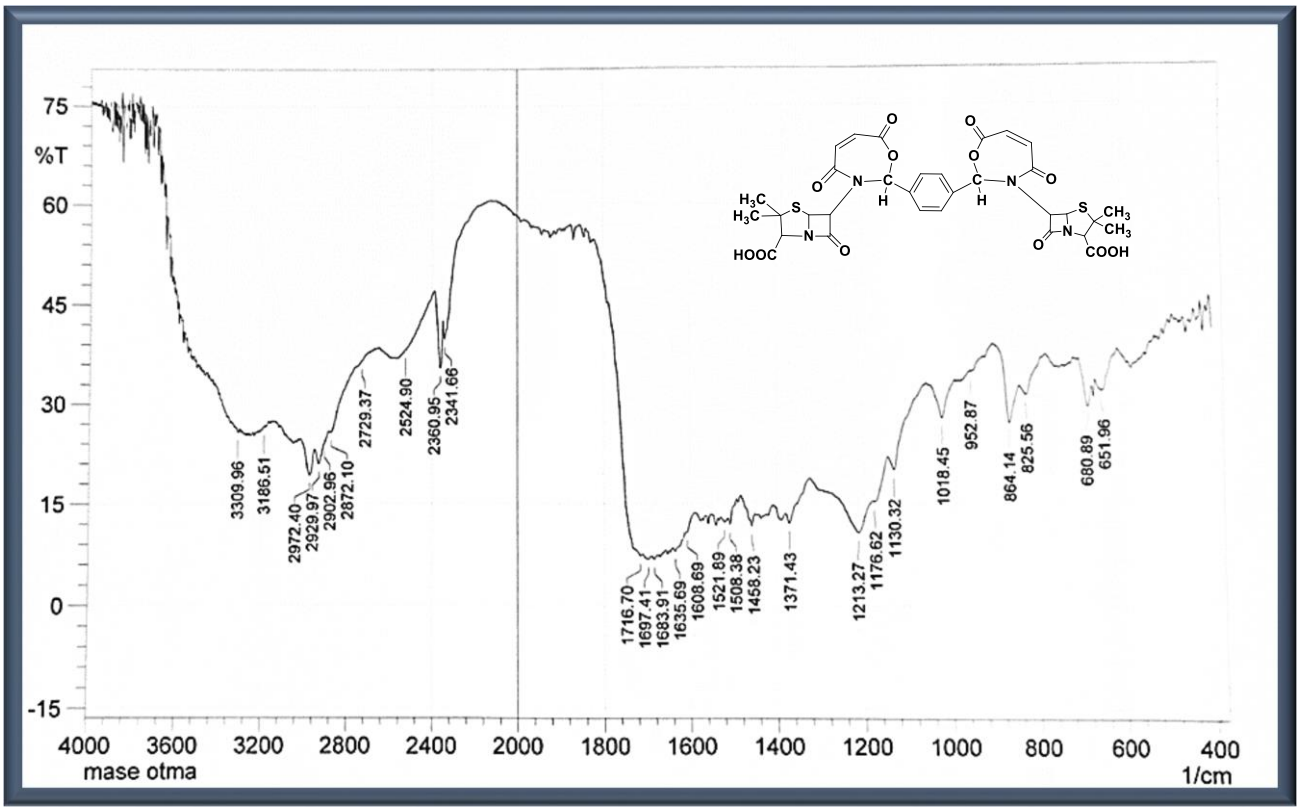


Fig (3-52): FTIR spectrum for (C6)

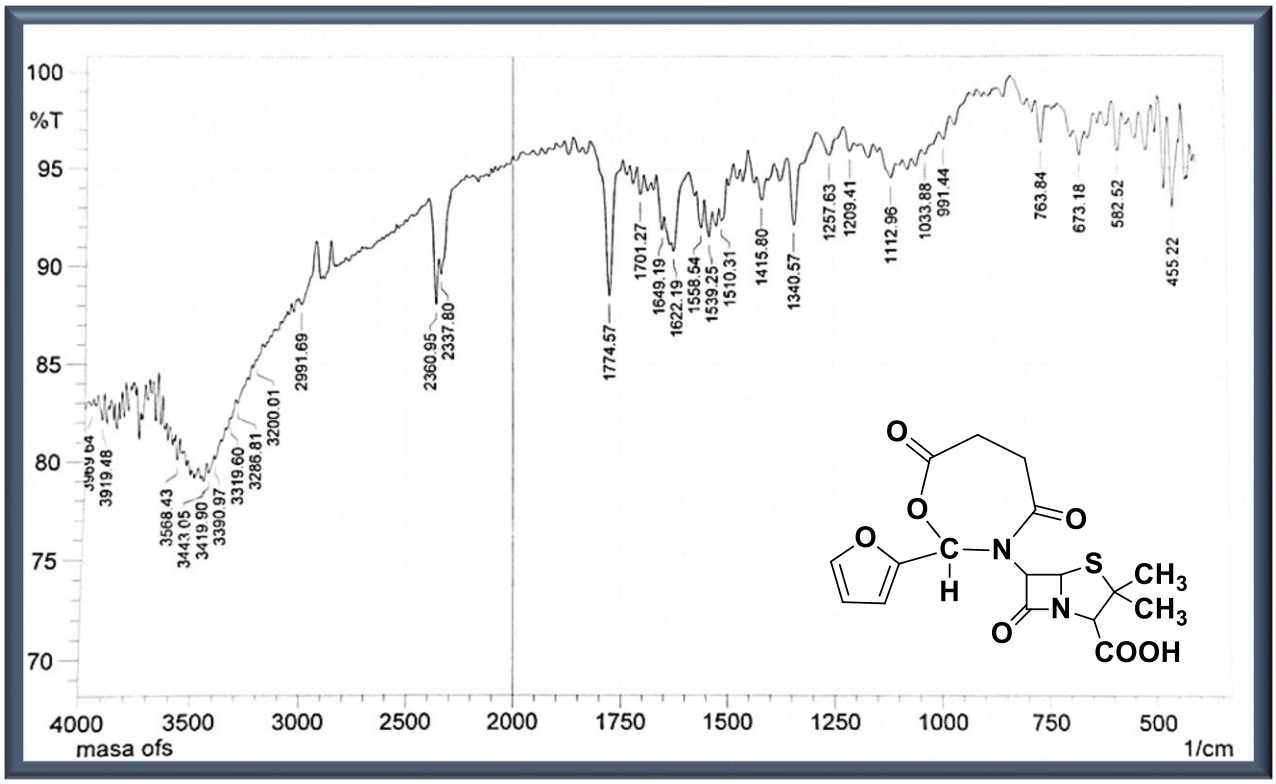


Fig (3-53): FTIR spectrum for (C7)

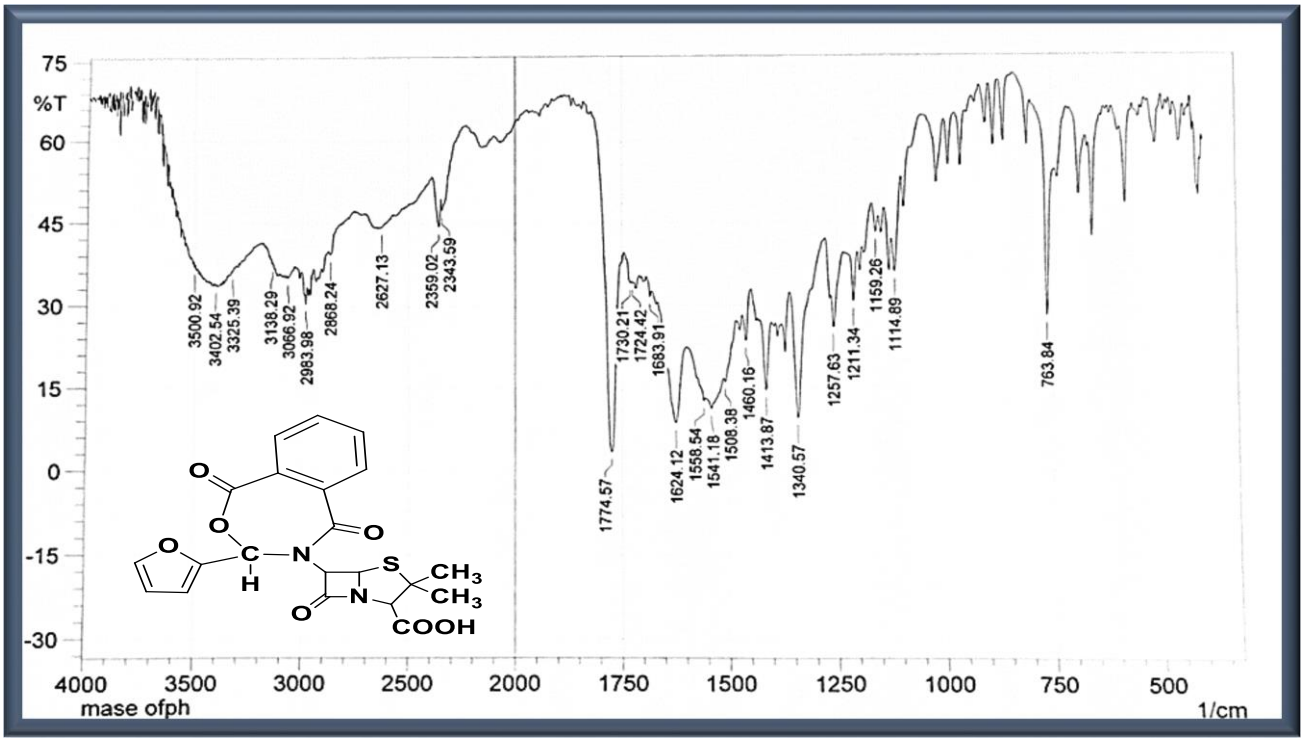


Fig (3-54): FTIR spectrum for (C8)

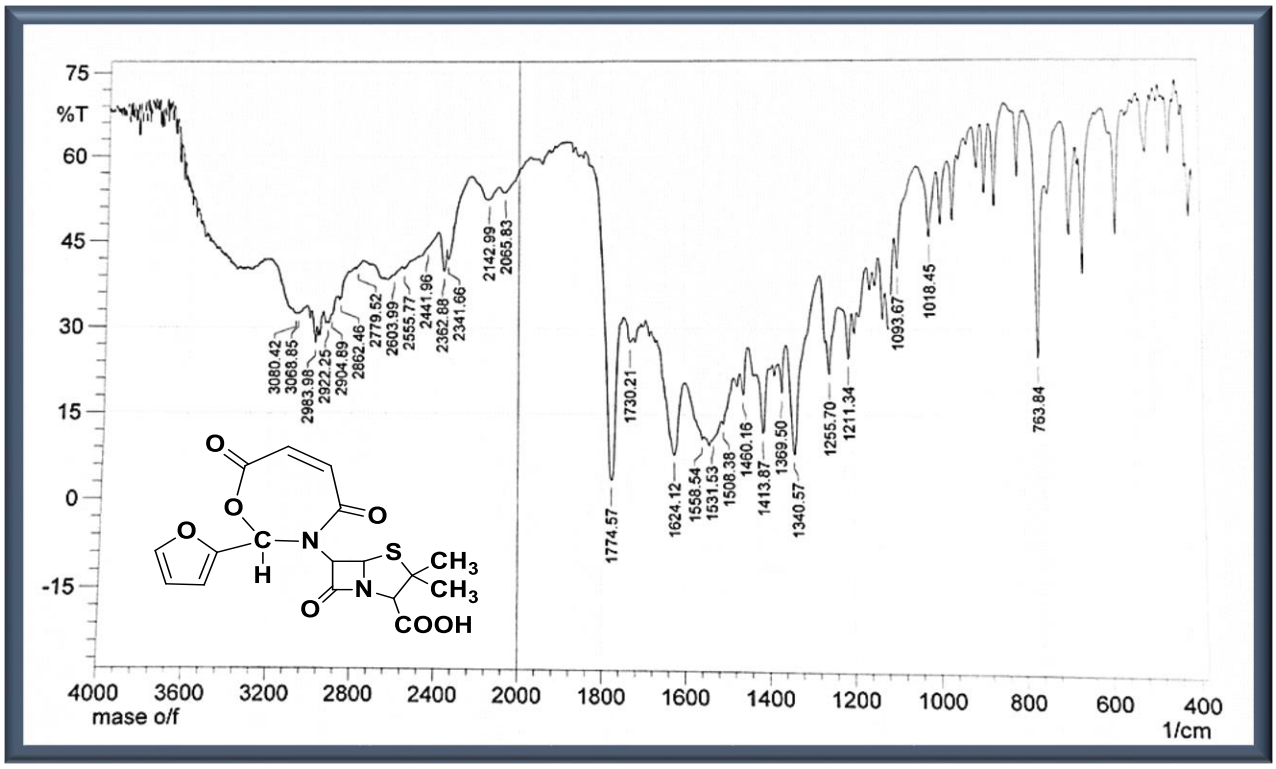


Fig (3-55): FTIR spectrum for (C9)

3.18. FT-IR Spectra of Complexes oxazepane's (D1, D2, D3, D4, D5, D6, D7, D8, D9):

The IR spectrum of the complexes change in this groups (C=O) lactam, Indicates coordination occur via the donation atom in this groups with Transition Metal Ion Zn (II).no change in this groups (O-H) and (C=O) Lactone noticed, the possibility that coordination occur via the donation atom in this group was excluded with Transition Metal Ion Zn (II), The IR spectrum of the complexes (D1,D2,D3,D4,D5,D6,D7,D8,D9) band at (550-450) cm^{-1} was assigned to the stretching vibration of υ(M-O)and(M-N)[Vinusha et al., 2019], As shown in the Table (3.8).

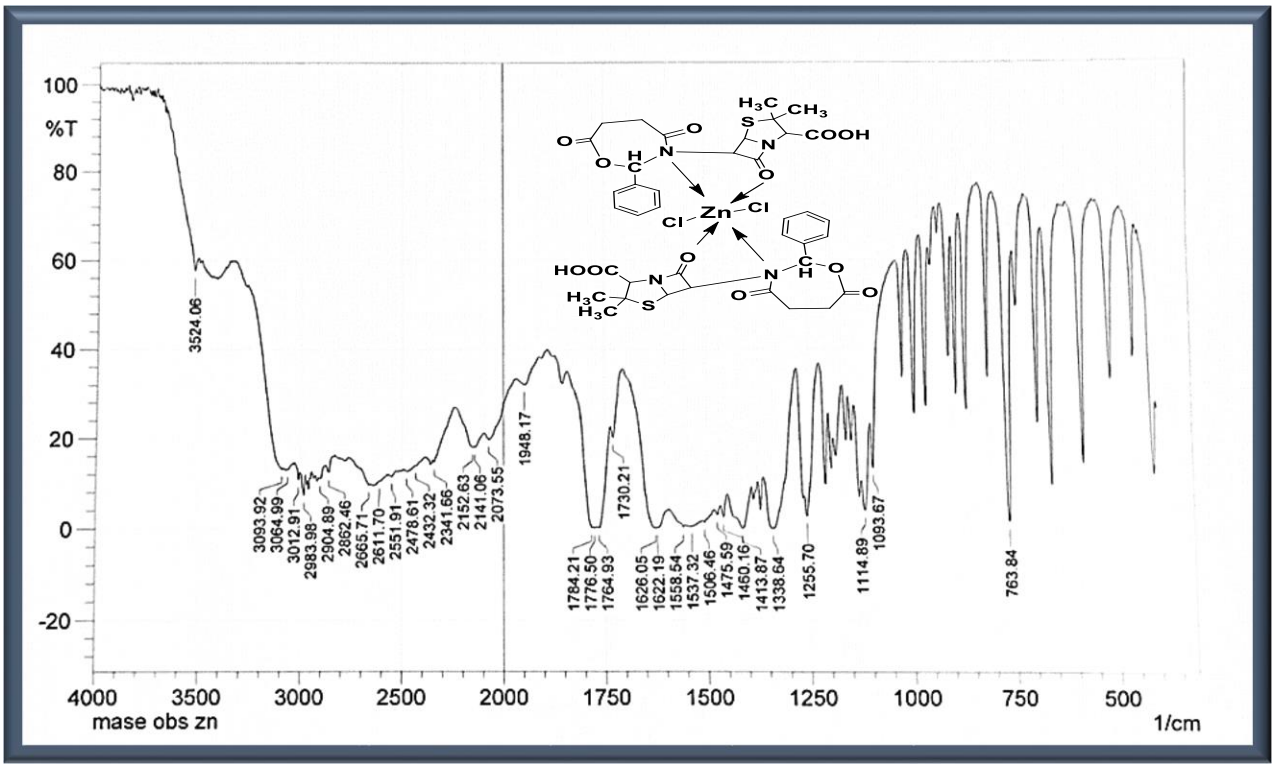


Fig (3-56): FTIR spectrum for (D1)

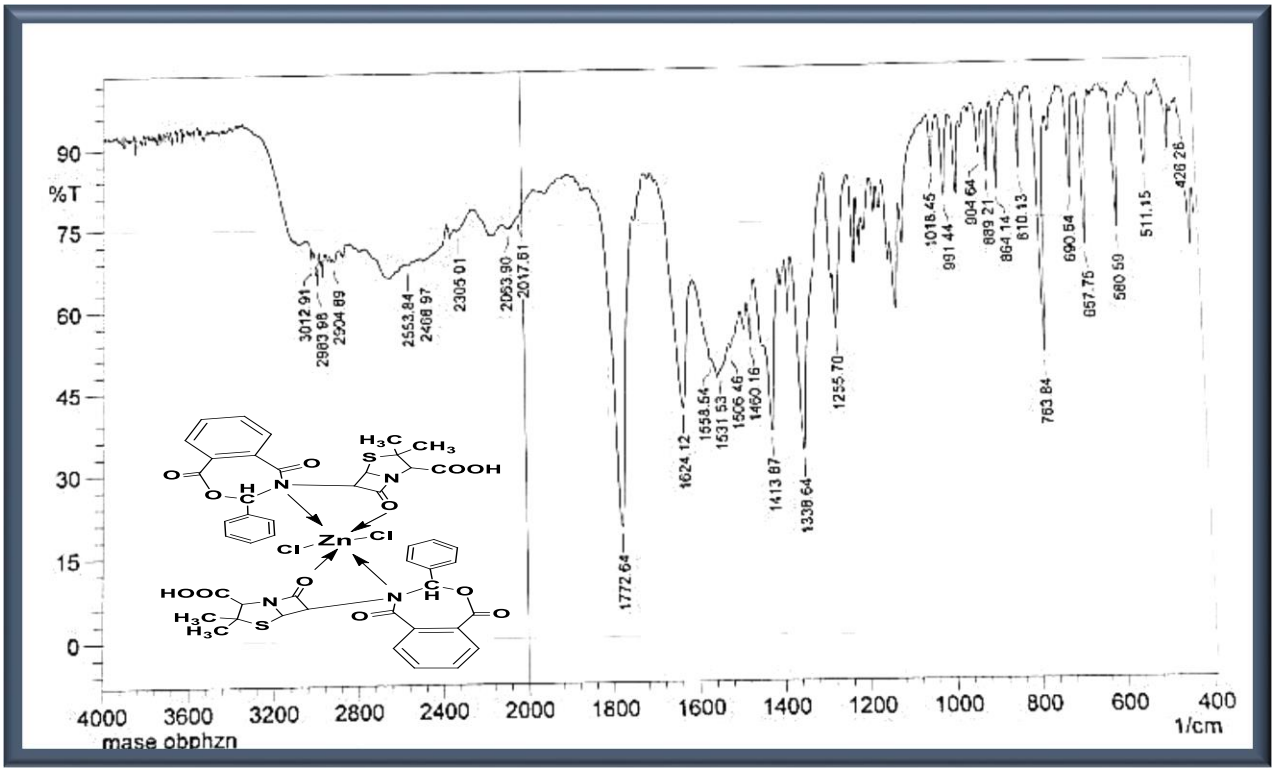


Fig (3-57): FTIR spectrum for (D2)

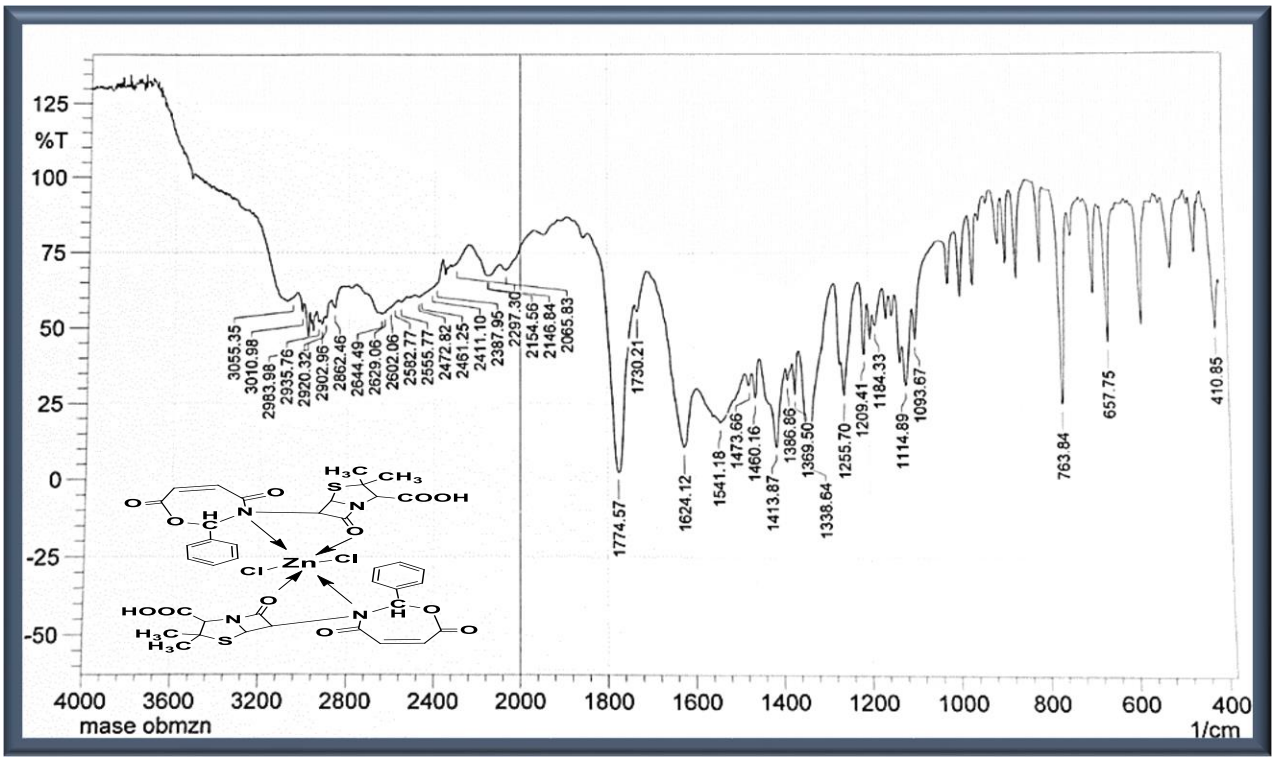


Fig (3-58): FTIR spectrum for (D3)

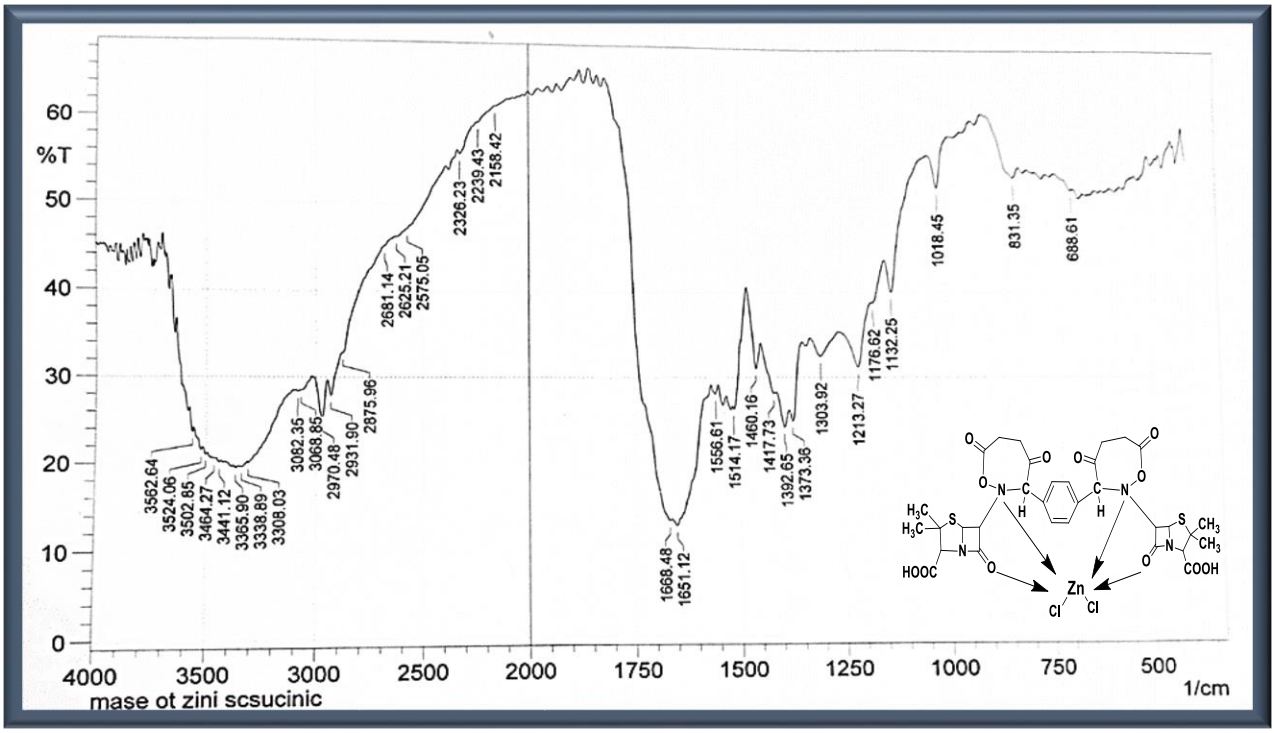


Fig (3-59): FTIR spectrum for (D4)

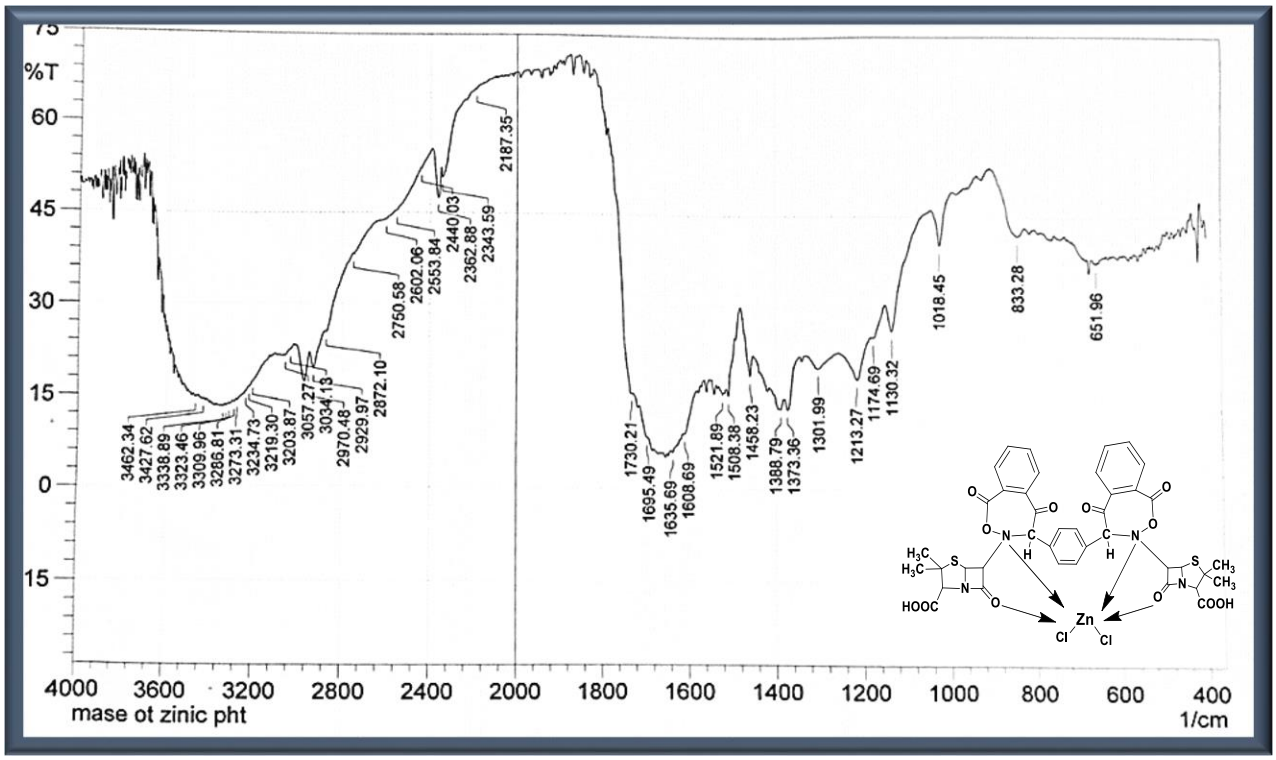


Fig (3-60): FTIR spectrum for (D5)

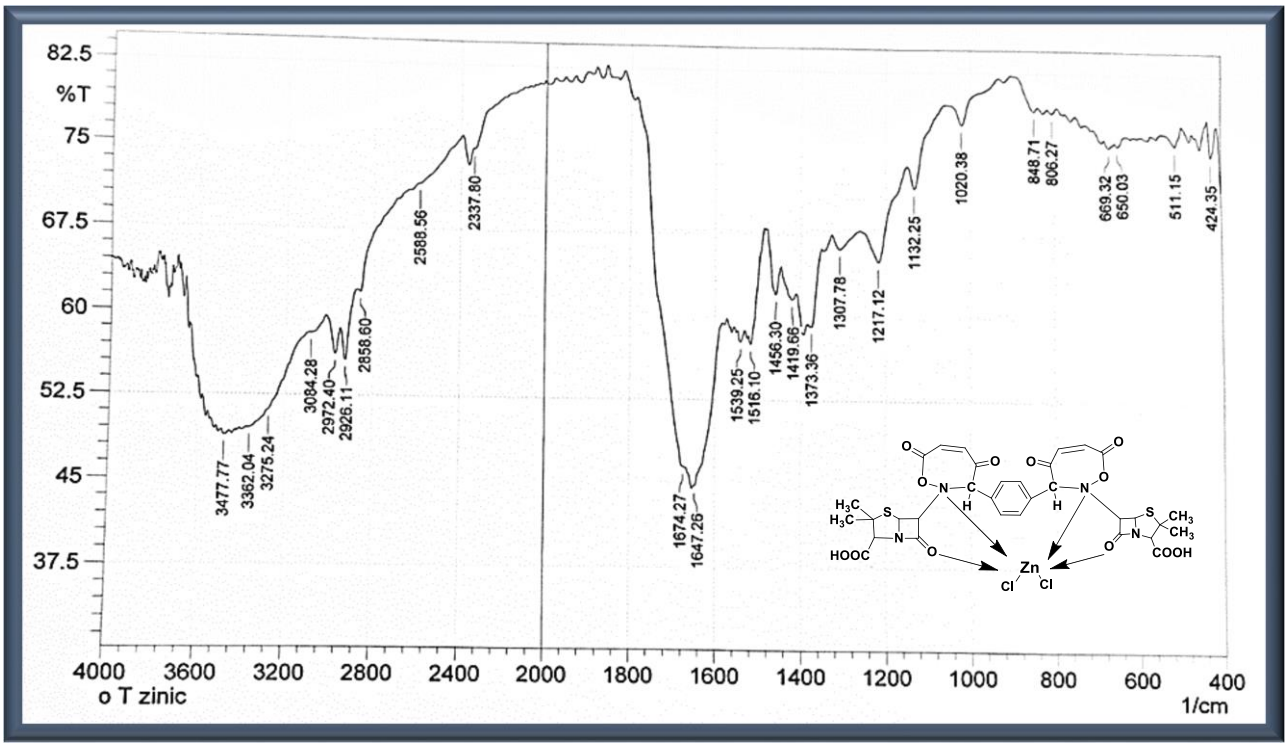


Fig (3-61): FTIR spectrum for (D6)

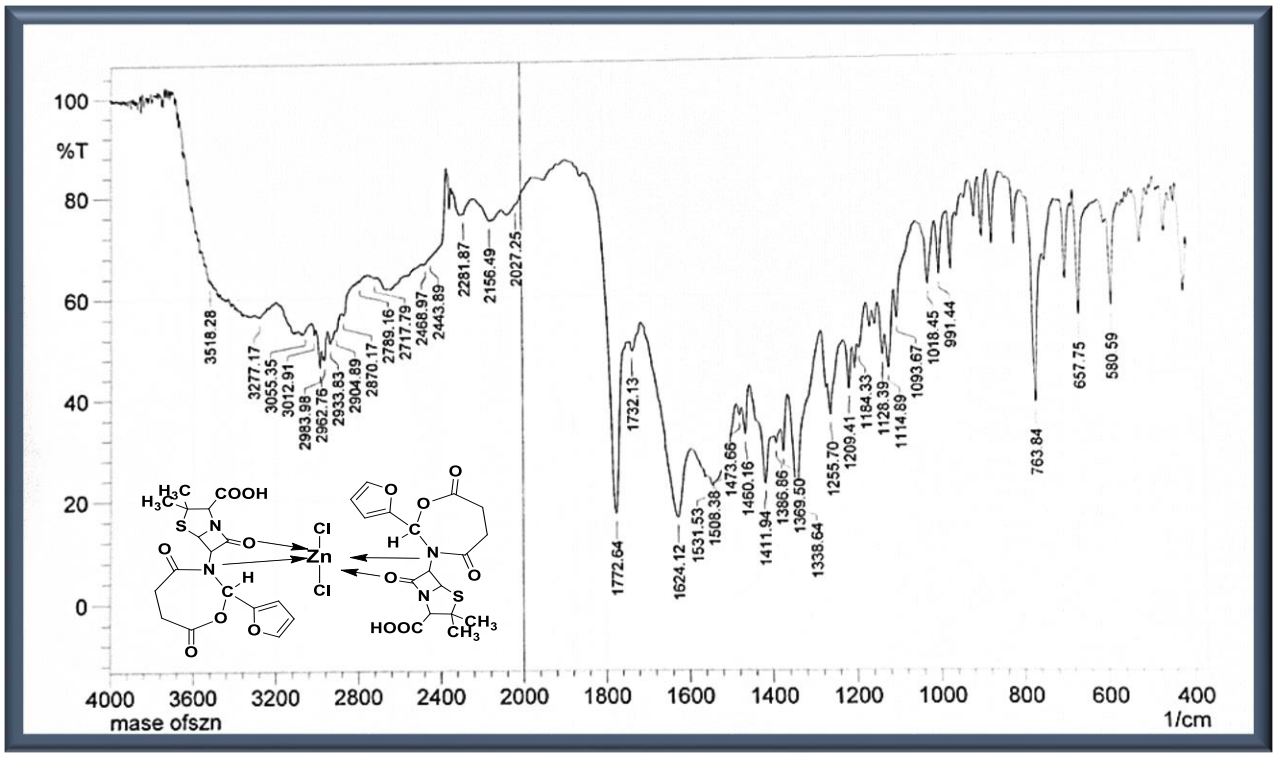


Fig (3-62): FTIR spectrum for (D7)

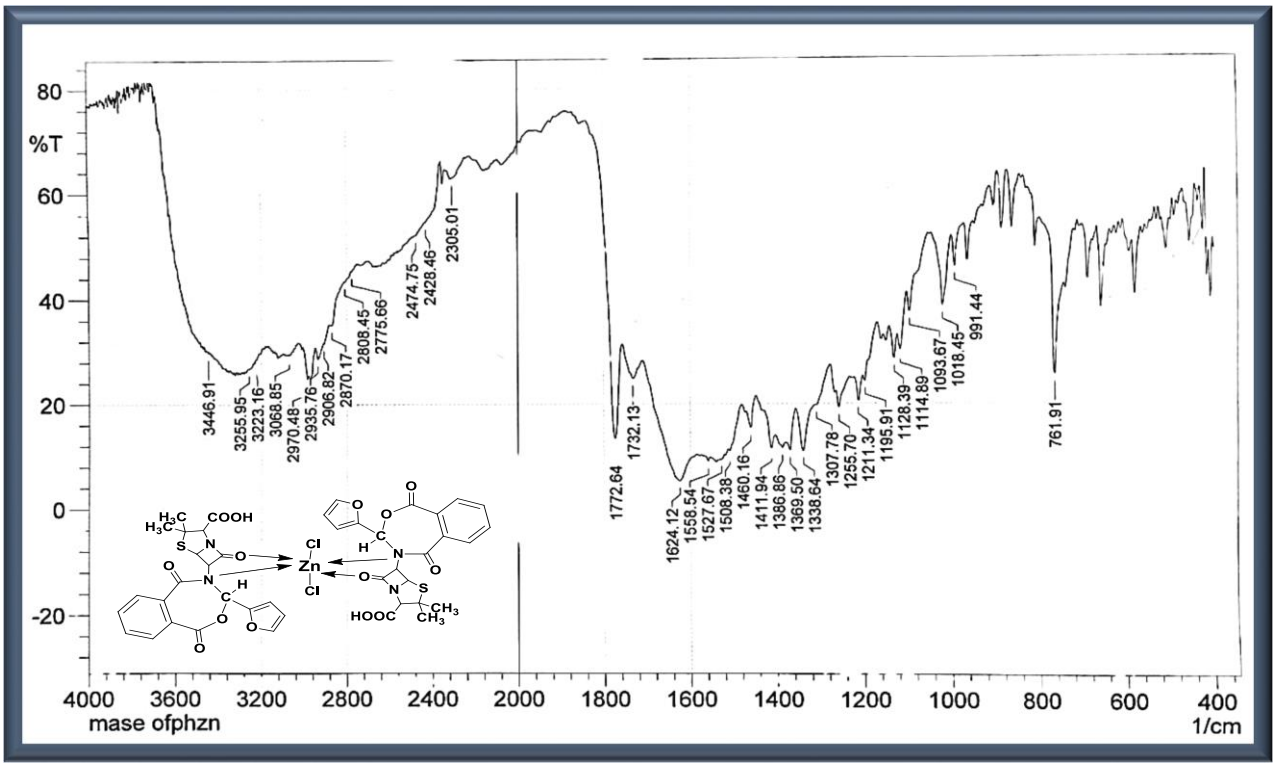


Fig (3-63): FTIR spectrum for (D8)

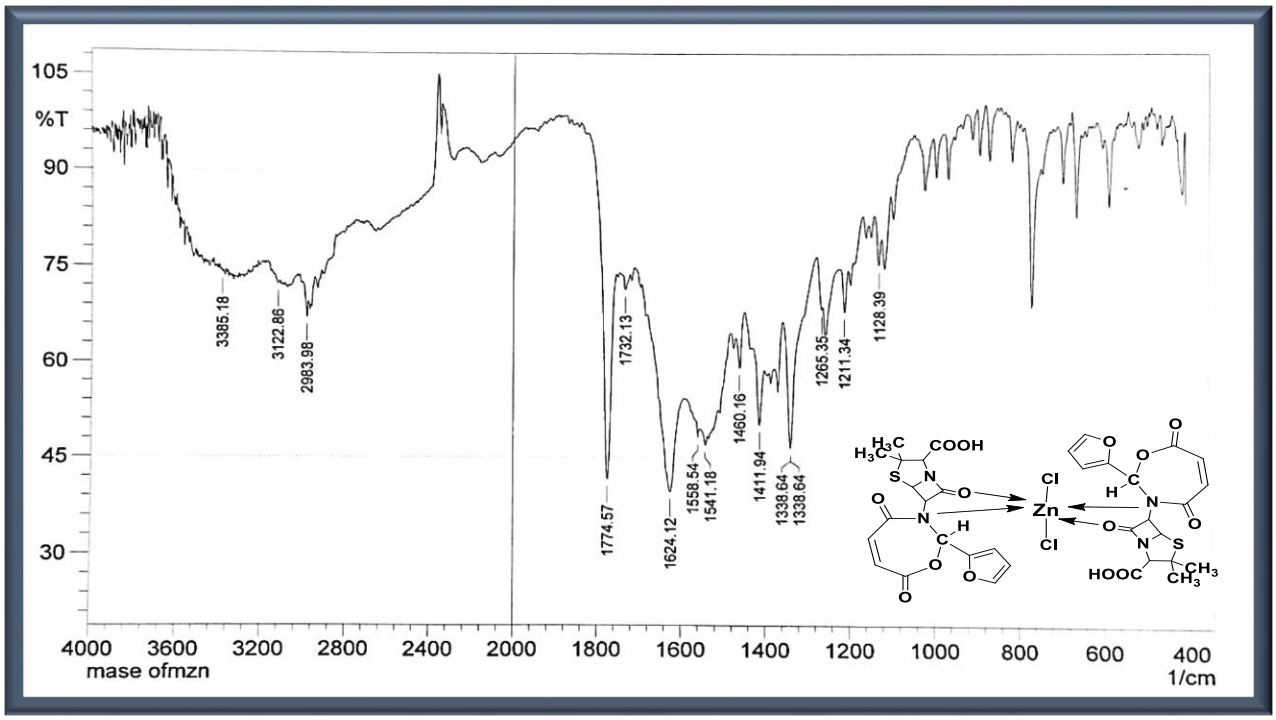


Fig (3-64): FTIR spectrum for (D9)

Table (3-9): the values of frequencies for the important bands in the

Compound	*O-H*	*C-H Aromatic*	*C=O Carboxyl*	*C=O Lactam*	*C=O Oxazepine*
C1	***3515***	***3055***	***1772***	***1722***	***1624***
C2	***3571***	***3066***	***1774***	***1750***	***1624***
C3	***3578***	***3012***	***1774***	***1716***	***1624***
C4	***3333***	***3053***	***1772***	***1693***	***1566***
C5	***3325***	***3061***	***1791***	***1764***	***1690***
C6	***3309***	***3186***	***1776***	***1697***	***1635***
C7	***3568***	***3200***	***1774***	***1701***	***1622***
C8	***3500***	***3066***	***1774***	***1724***	***1624***
C9	***3385***	***3068***	***1774***	***1732***	***1624***
D1	***3524***	***3093***	***1776***	***1764***	***1626***
D2	***3575***	***3012***	***1772***	***1767***	***1624***
D3	***3531***	***3055***	***1774***	***1730***	***1624***
D4	***3562***	***3082***	***1774***	***1668***	***1556***
D5	***3462***	***3057***	***1793***	***1730***	***1689***
D6	***3477***	***3084***	***1774***	***1674***	***1647***
D7	***3500***	***3055***	***1774***	***1724***	***1624***
D8	***3446***	***3068***	***1772***	***1732***	***1624***
D9	***3422***	***3122***	***1774***	***1742***	***1624***

infrared spectrum of the oxazepane's and complexes oxazepane's

3.19.Characterization Compounds by Mass Spectroscopy:

Mass spectrometry has been used successfully to study molecular structures [Prakash et.al., 2010],The structure of substances is further supported by data collected from mass spectral analysis for further inquiry. The mass spectra for all of the target compounds (Table 3.9) show that .The computed values for the m/z ratio have been quite close to the values of Figures below represent m/z measurements.

Table 3.10. Show to fragmentation for oxazepane's

C1		C4		C7	
m/z	**Abundance**	**m/z**	**Abundance**	**m/z**	**Abundance**
41.2	***312384***	***51.3***	***1290.7***	***44.1***	***1040704***
75.1	***651072***	***76.0***	***28437.1***	***75.2***	***610112***
114.1	***523904***	***104.0***	***27743.9***	***98.2***	***277184***
138.2	***162304***	***167.0***	***6787.9***	***127.1***	***19920***
160.1	***989056***	***231.9***	***14382.2***	***160.2***	***494784***
183.2	***217216***	***314.9***	***5316.8***	***183.2***	***42736***
216.1	***76792***	***371.1***	***1742.7***	***216.1***	***24704***
263.1	***29496***	***578.1***	***1730.2***	***281***	***1635***
366.3	***7499***	***630.5***	***1645.0***	***327.1***	***638***
404.6	***986***	***736.5***	***1755.1***	***394.7***	***275***

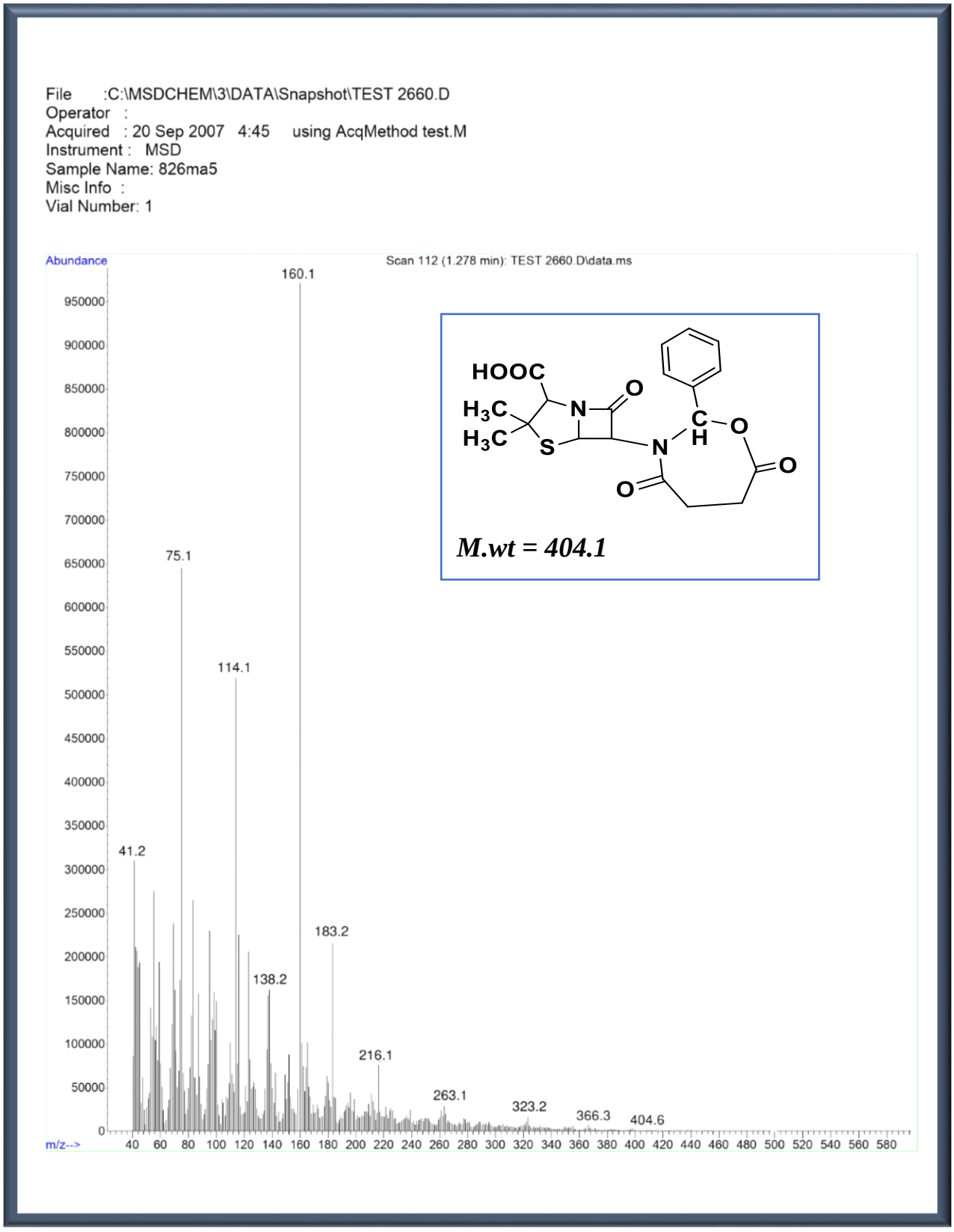


Fig. (3.65) Mass Spectra of C1

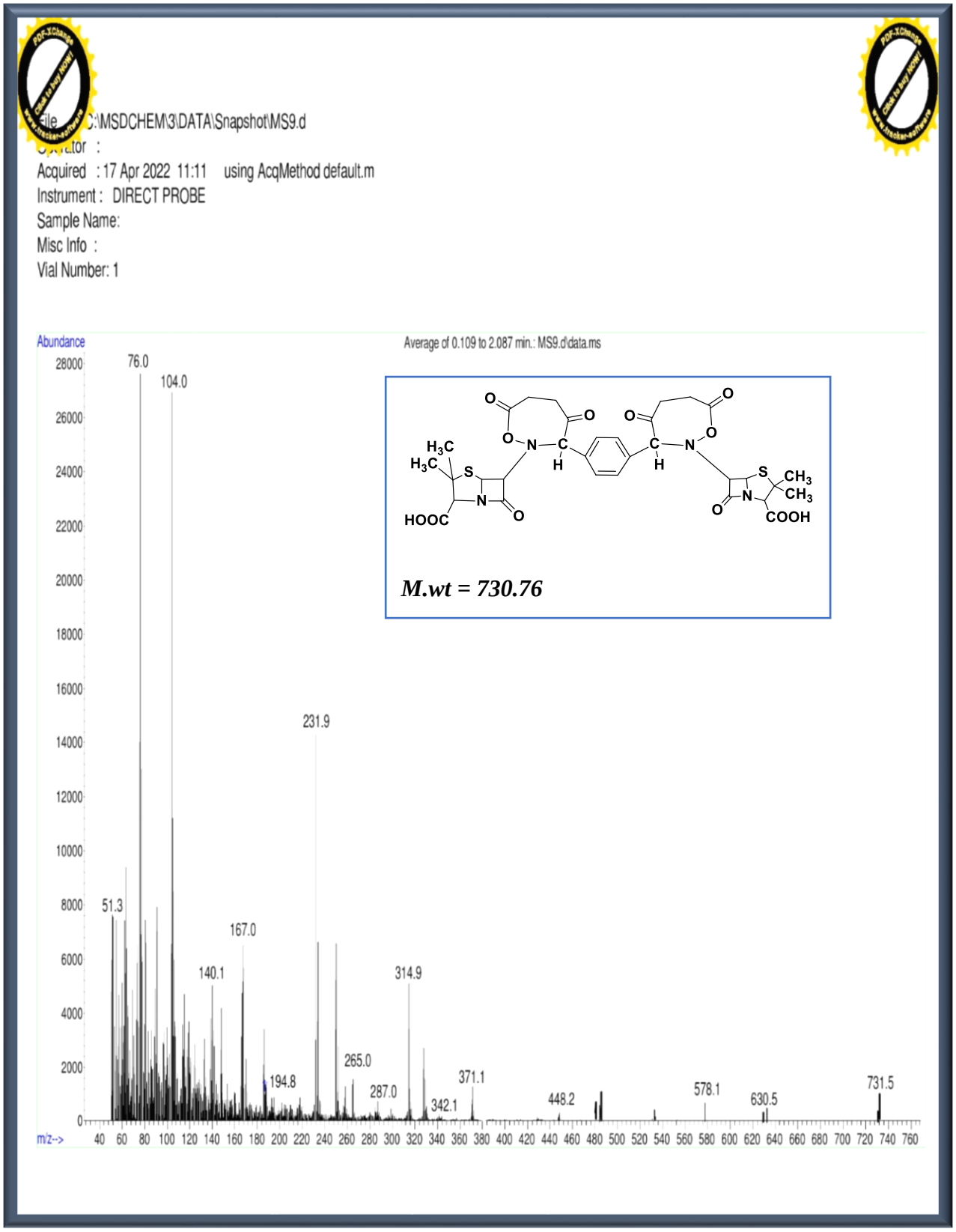


Fig. (3.66) Mass Spectra of C4

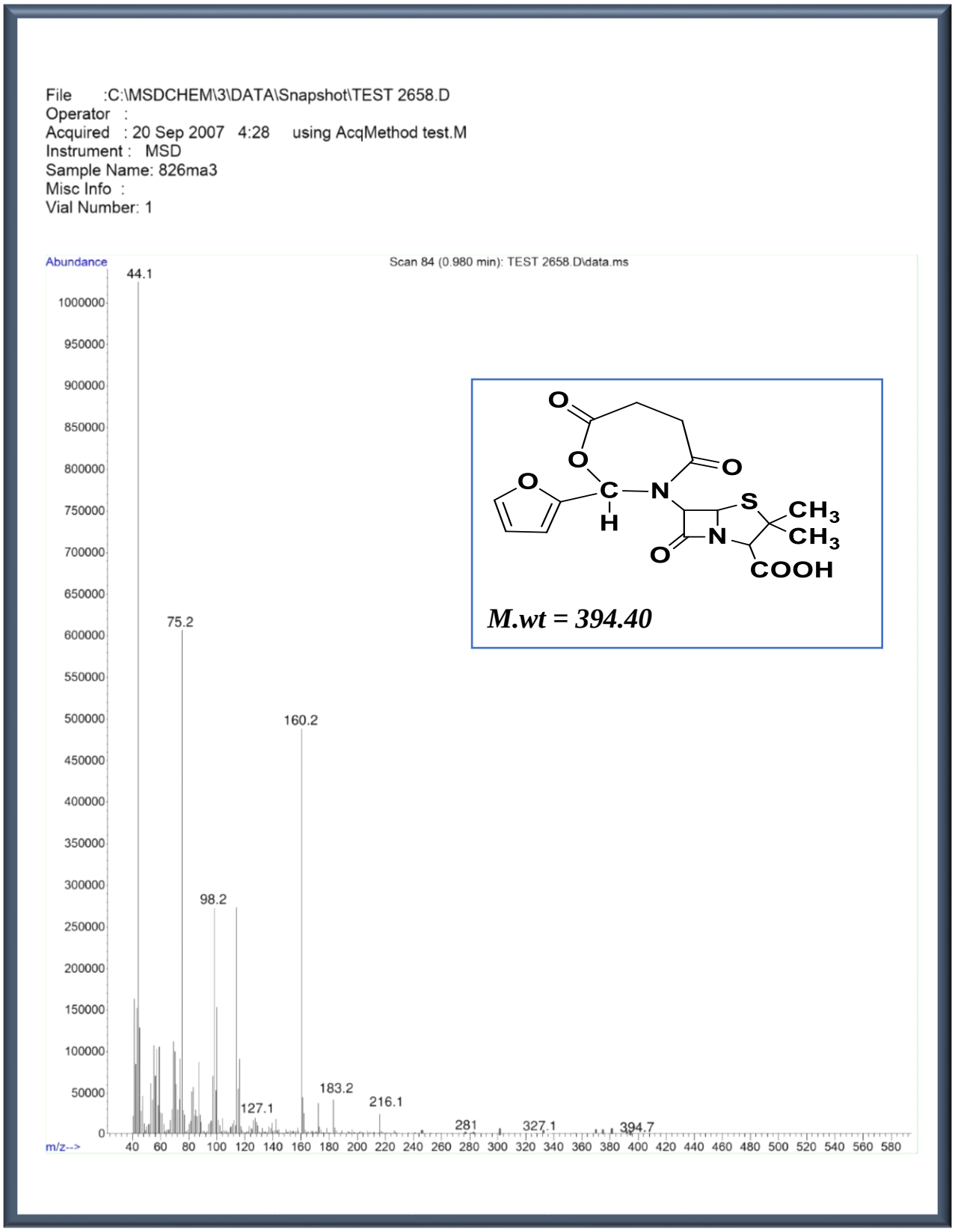


Fig. (3.67) Mass Spectra of C7

3.20.[1]H-NMR Spectra of the oxazepine's:

The [1]H-NMR spectrum of the oxazepine's figures below. The DMSO-d[6] solvent was showed a signal at (2.5ppm) and the first signal at δ=(1.1-1.5)ppm due (CH[3]) groups and signals in the range (4.5-4.8) ppm to the proton of the carbon atom bearing the carboxylic group(Abid and Ramadan, 2018), and the signals at δ=(10-11)ppm due (OH) groups of the oxazepine's (Jasim *et.al.*, 2020).

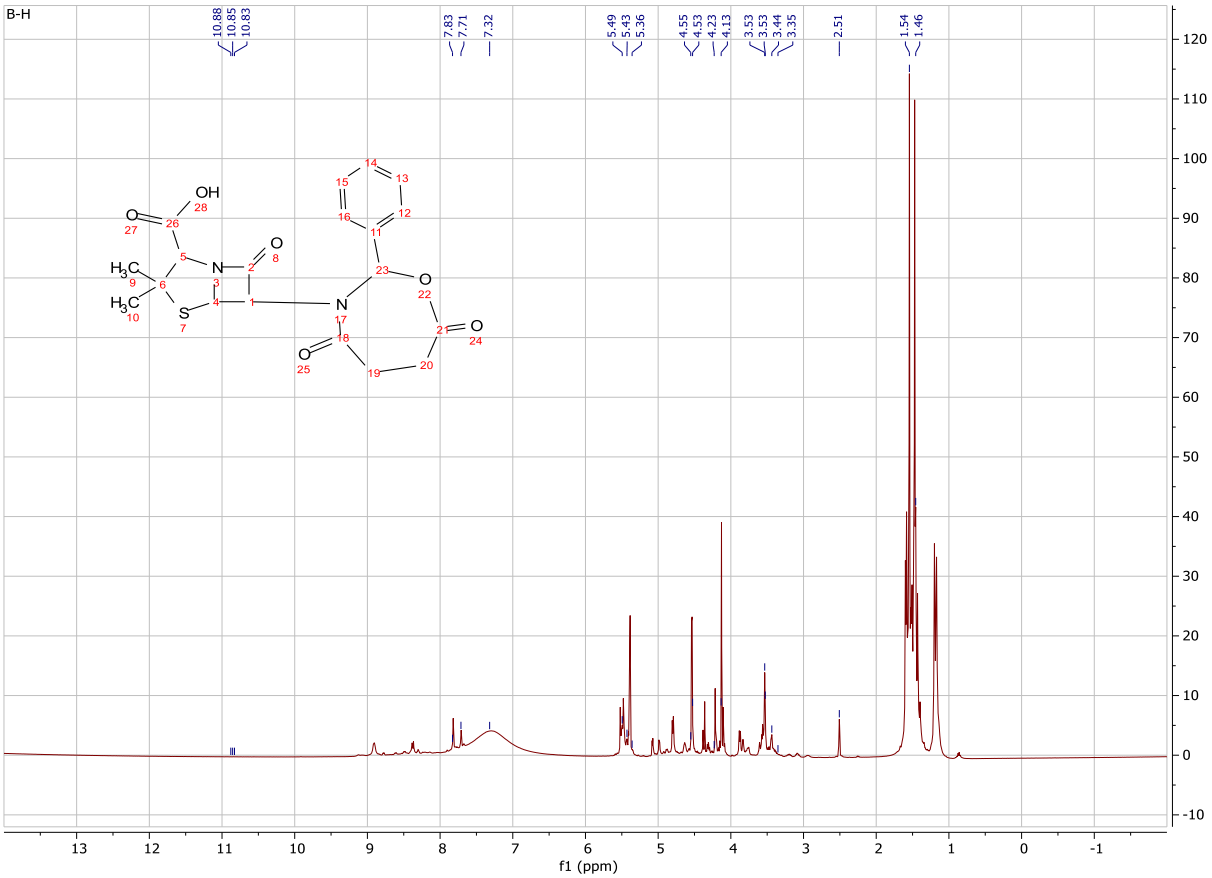


Fig (3.68)[1]HNMR Spectra of C1

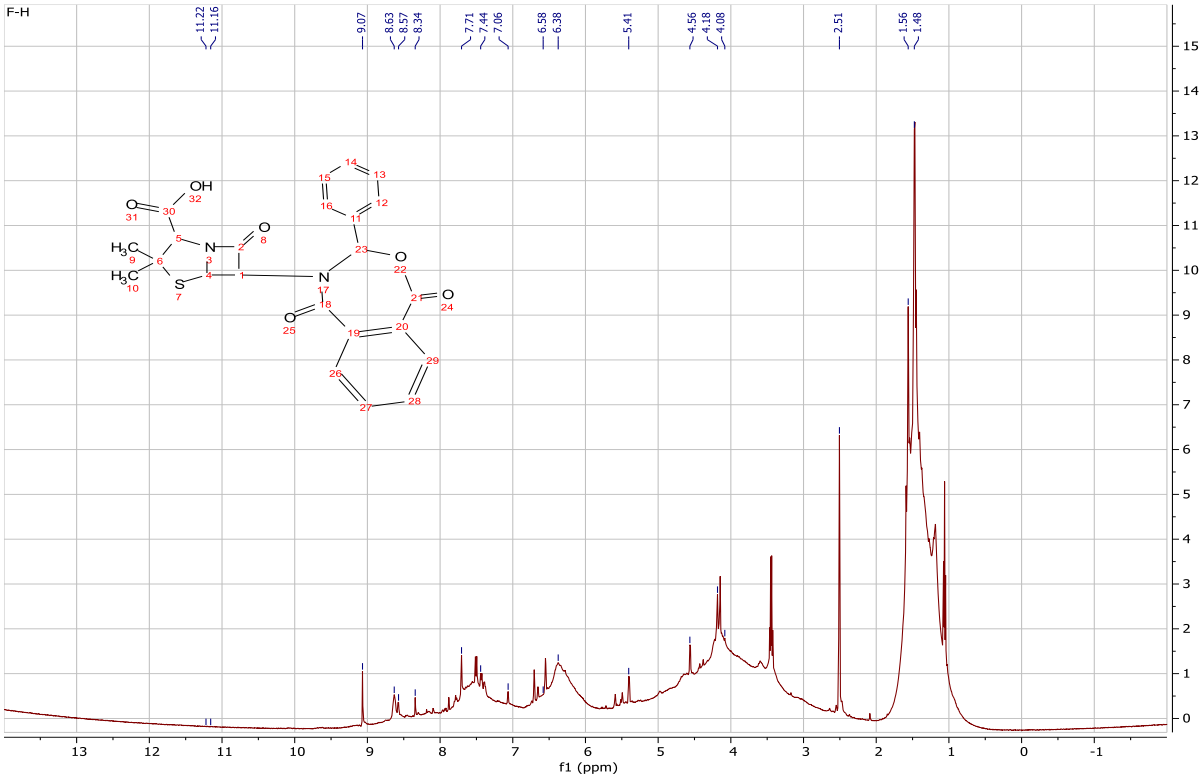


Fig (3.69)[1]HNMR Spectra of C2

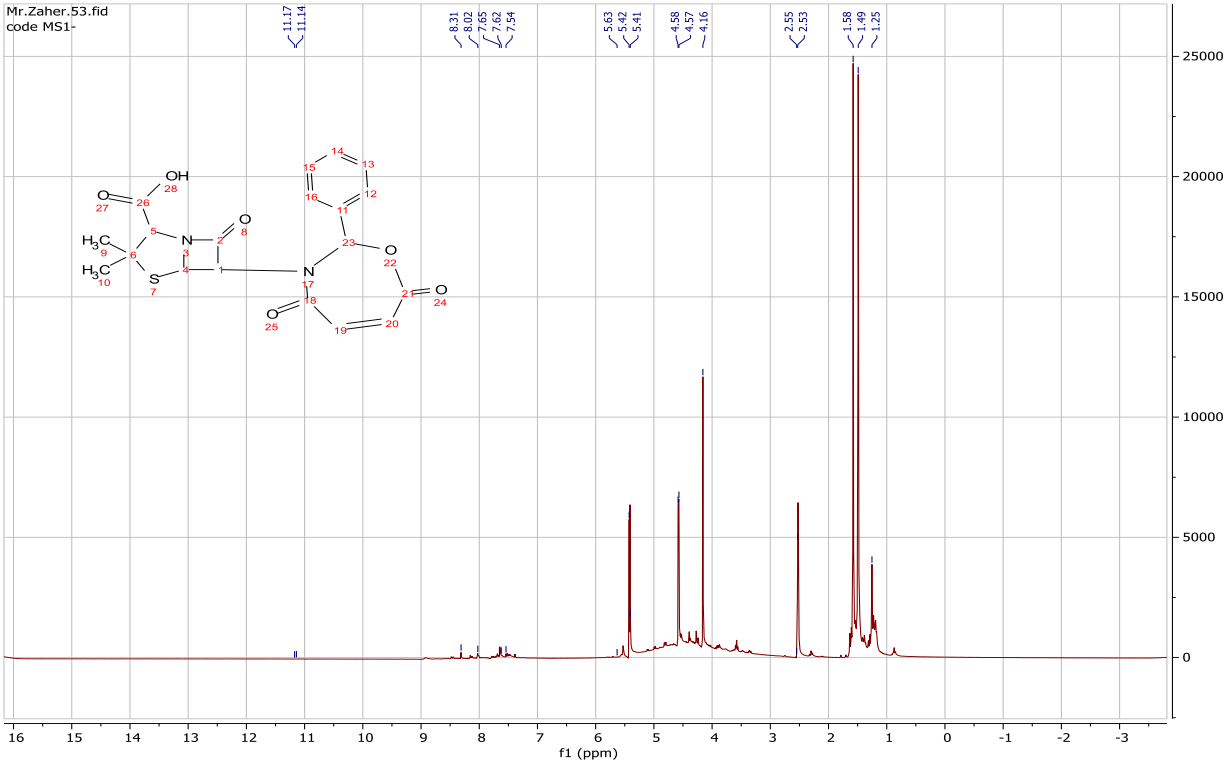


Fig (3.70)[1]HNMR Spectra of C3

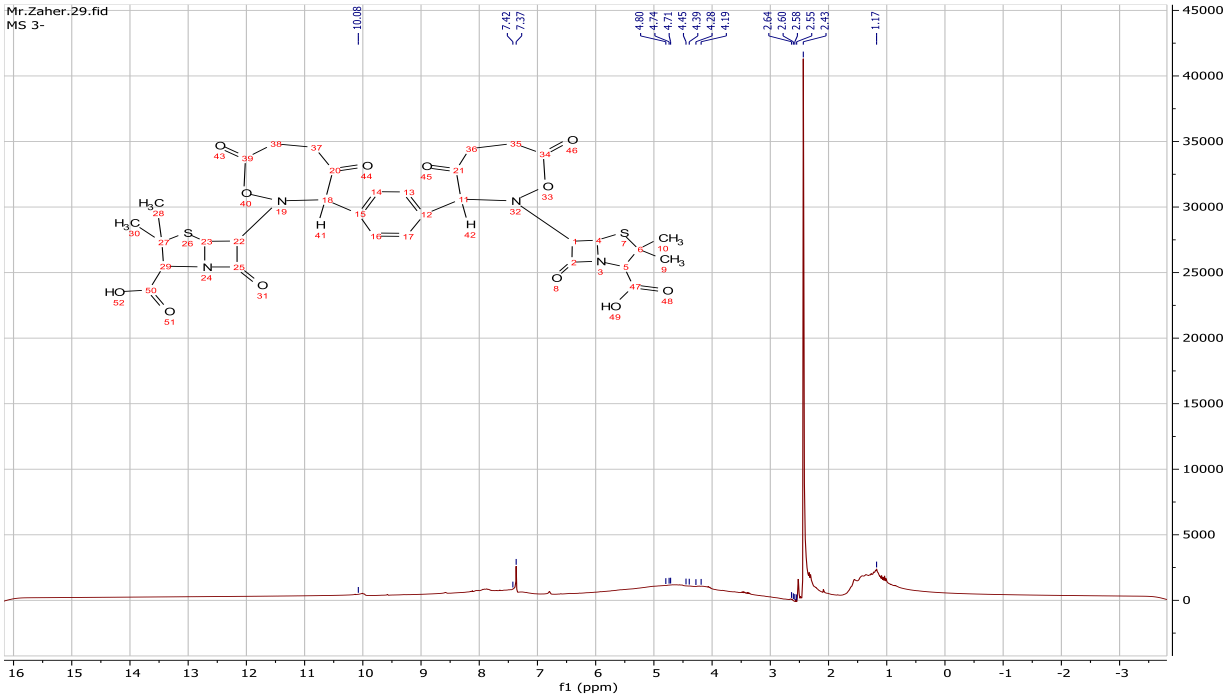


Fig (3.71)[1]HNMR Spectra of C4

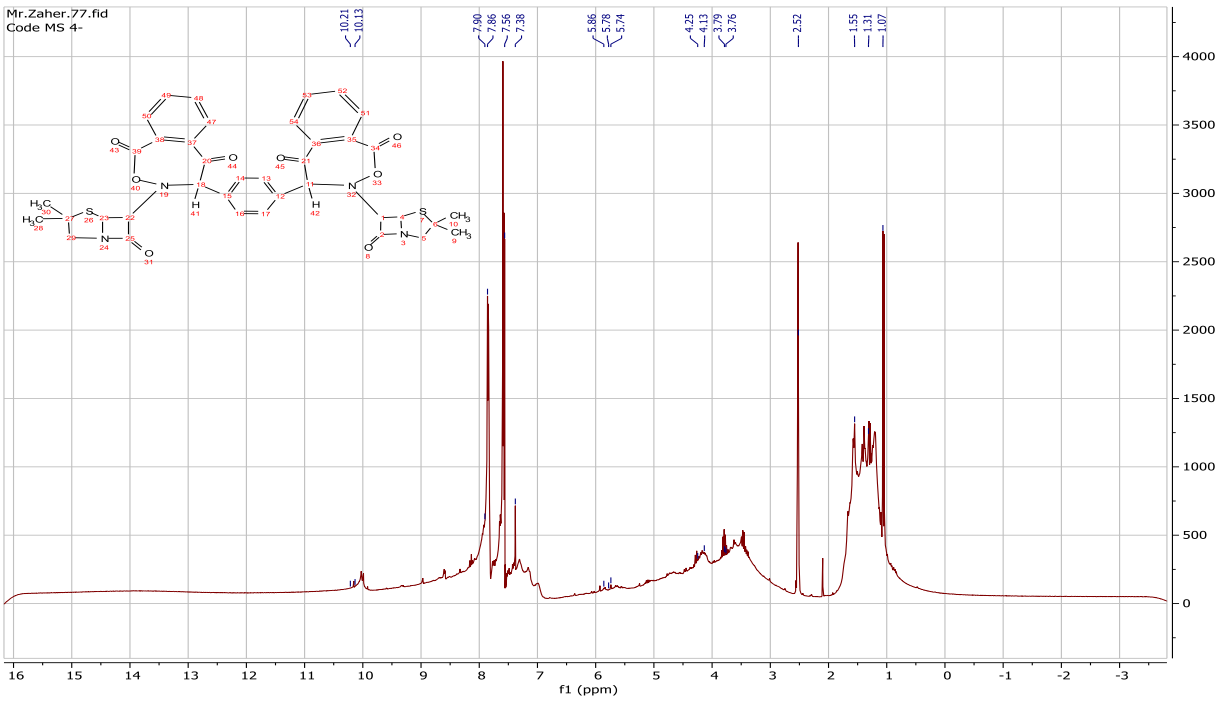


Fig (3.72)[1]HNMR Spectra of C5

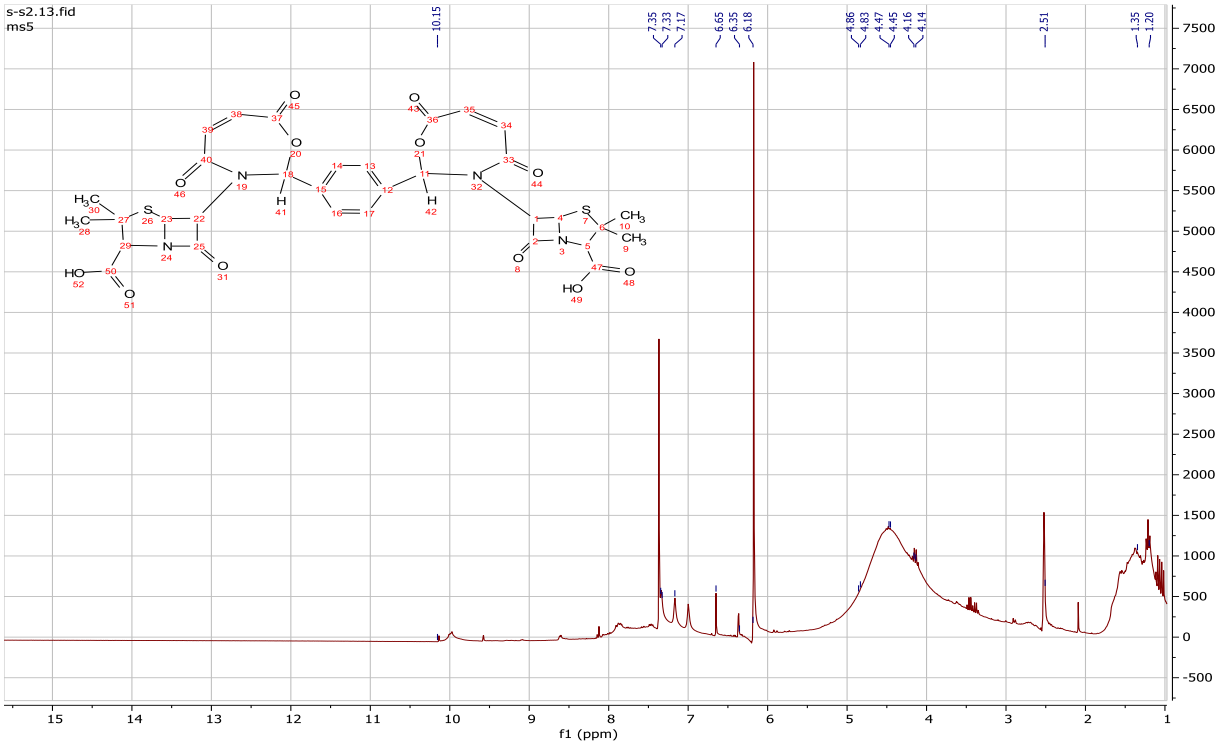


Fig (3.73)[1]HNMR Spectra of C6

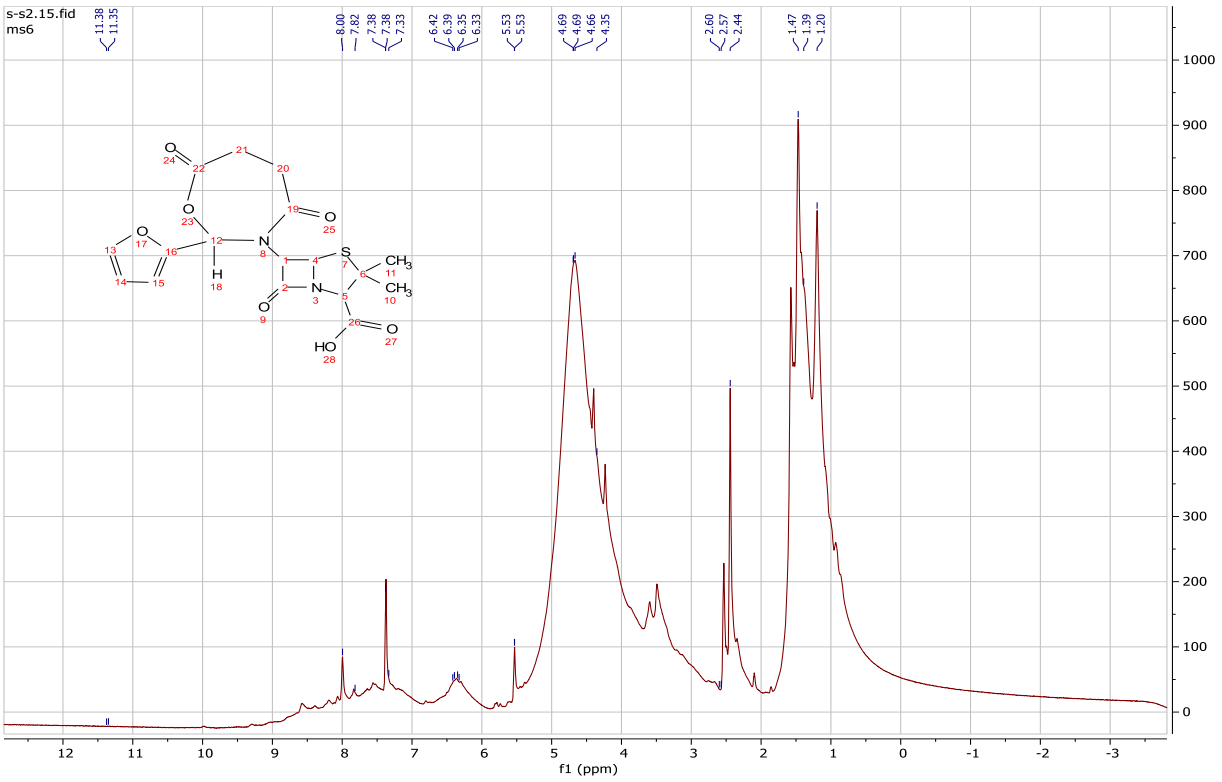


Fig (3.74)[1]HNMR Spectra of C7

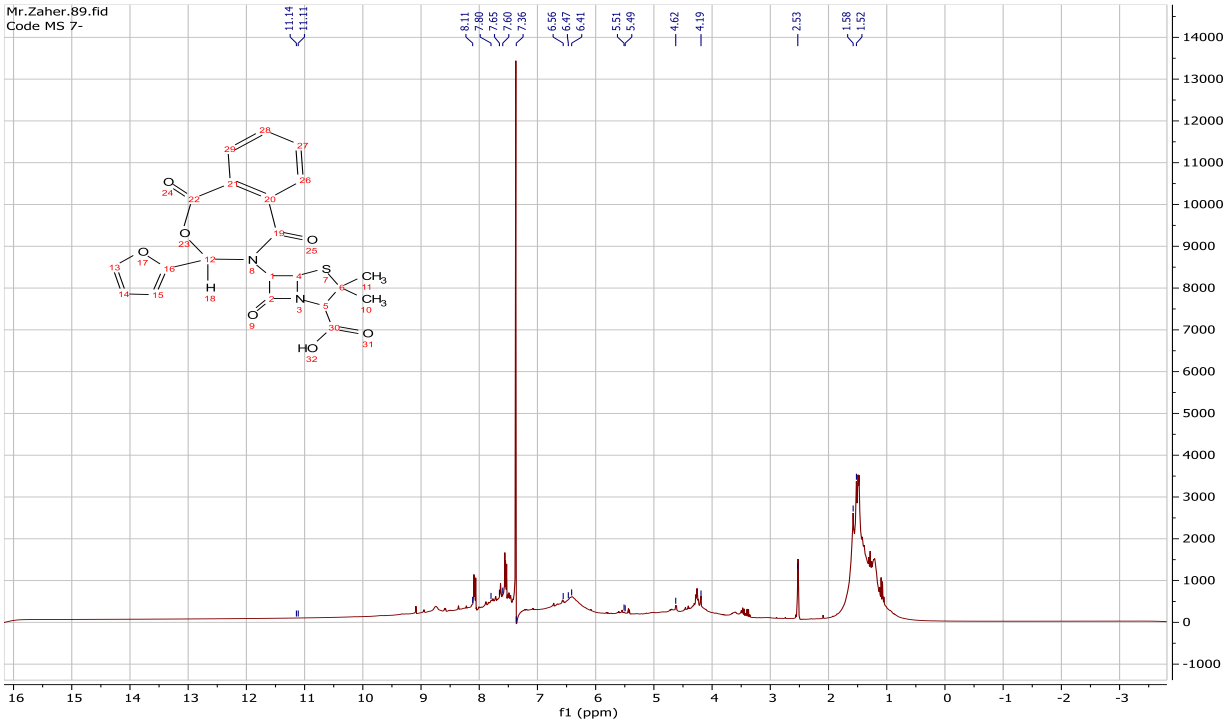


Fig (3.75)[1]HNMR Spectra of C8

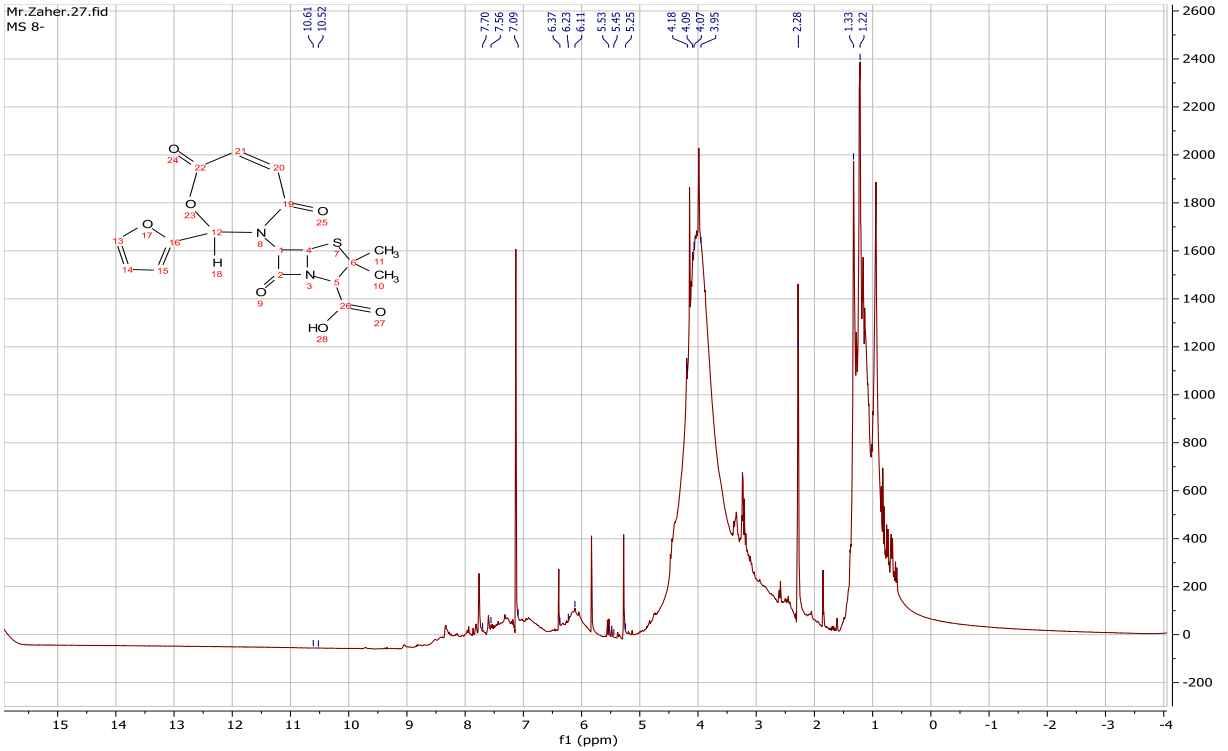


Fig (3.76)[1]HNMR Spectra of C9

3.21. ^{13}C-NMR Spectra of the oxazepine's:

The ^{13}CNMR the oxazepine's spectrum was recorded DMSO-d6 solvent was showed a signal at (40 ppm) [M.N. Ibrahim *et.al.*, 2011]. Figures below the ^{13}CNMR spectrum of oxazepine's (C1, C2, C3, C4, C5, C6, C7, C8, C9) showed the (N-C=O) at (160-165) ppm and (O-C=O) at (164-170) ppm [Essa and Al-Hamdani, 2018]. The (C=O) carboxylic group peak showed at (165-170) (M.N. Ibrahim *et.al.*, 2011). The (CH_3)group peak showed at (25-30) ppm [Muslim *et. al.*, 2018].

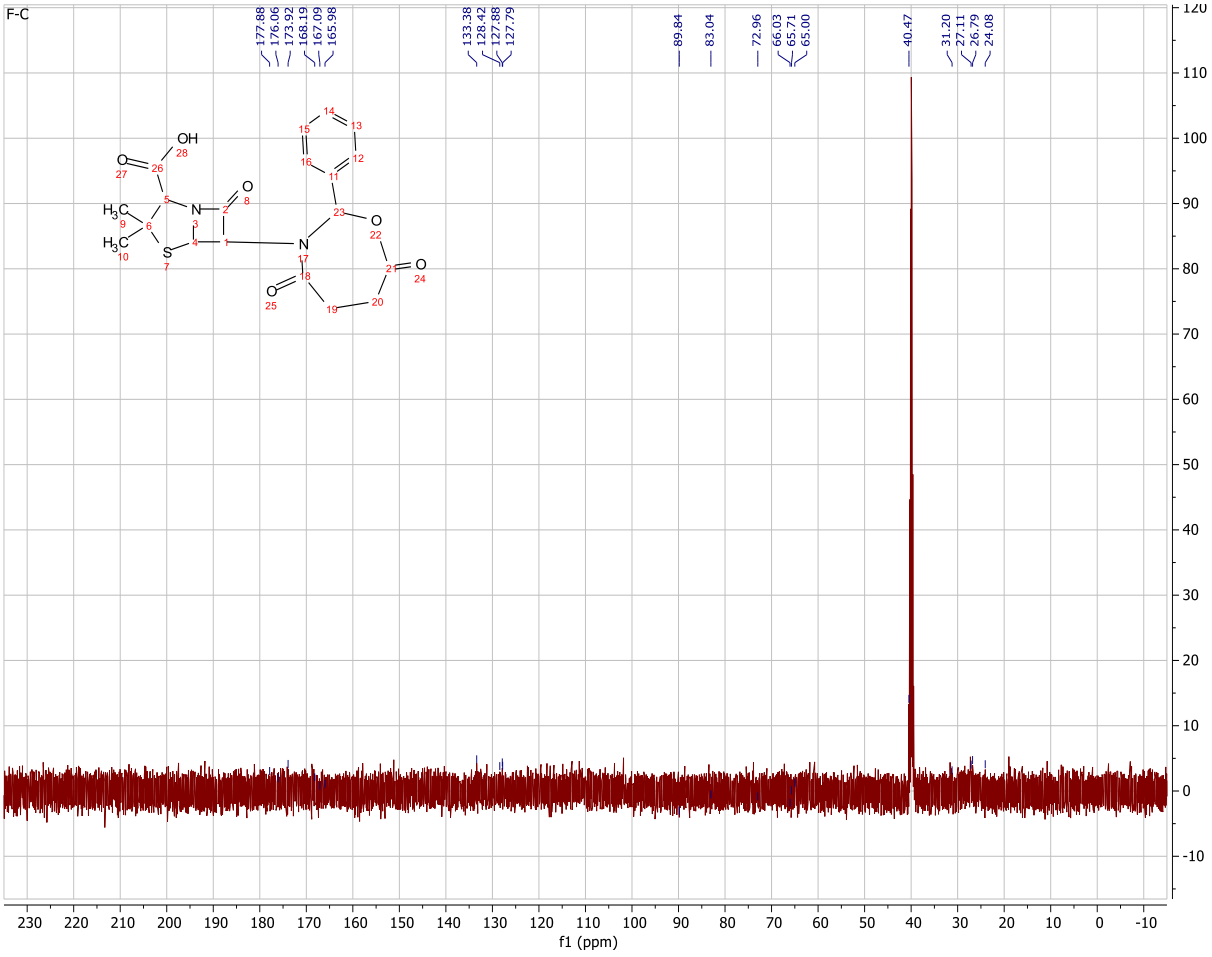


Fig. (3.77)^{13}CNMR Spectra of C1

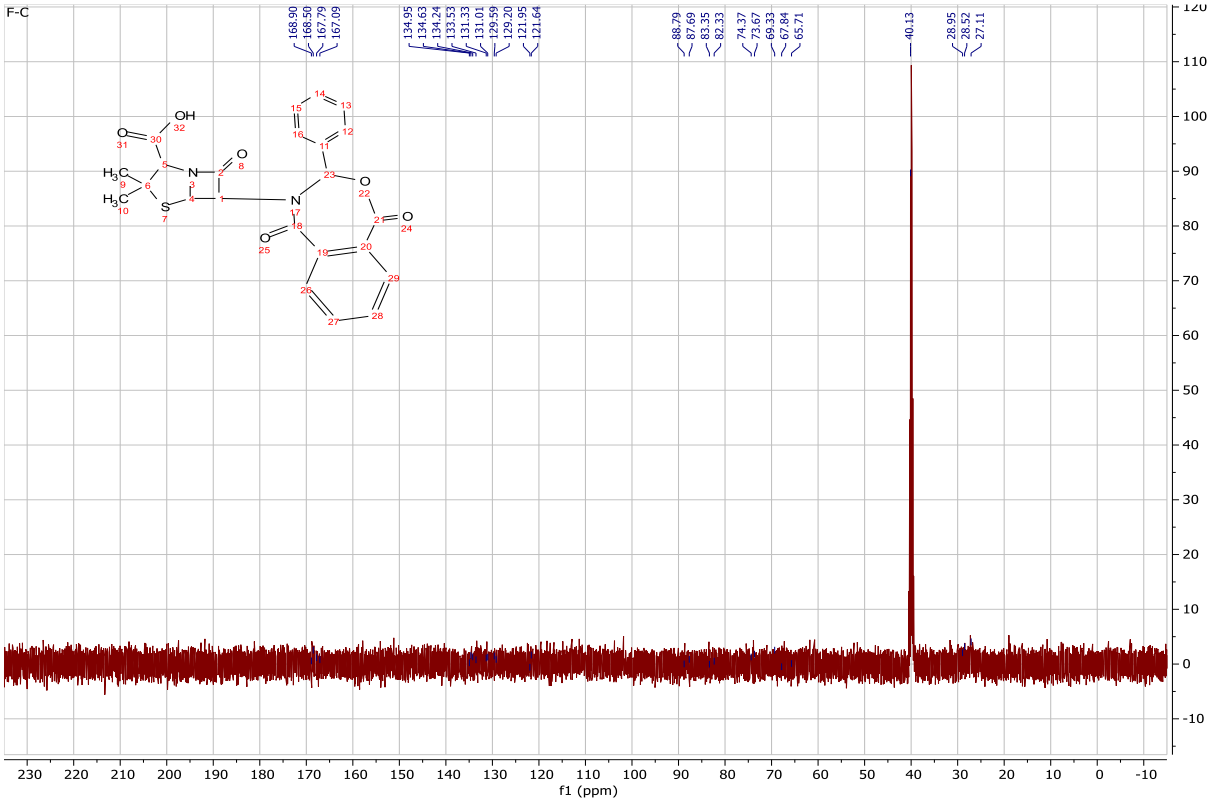


Fig. (3.78)^{13}CNMR Spectra of C2

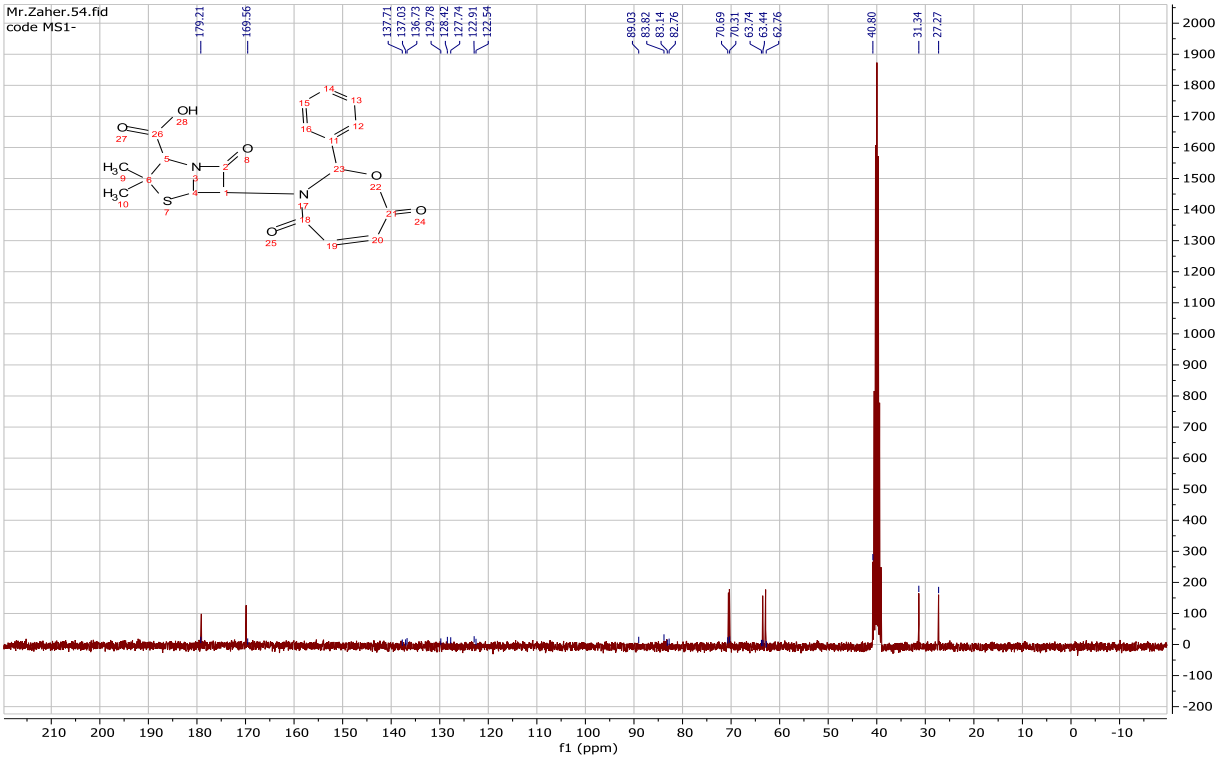


Fig. (3.79)^{13}CNMR Spectra of C3

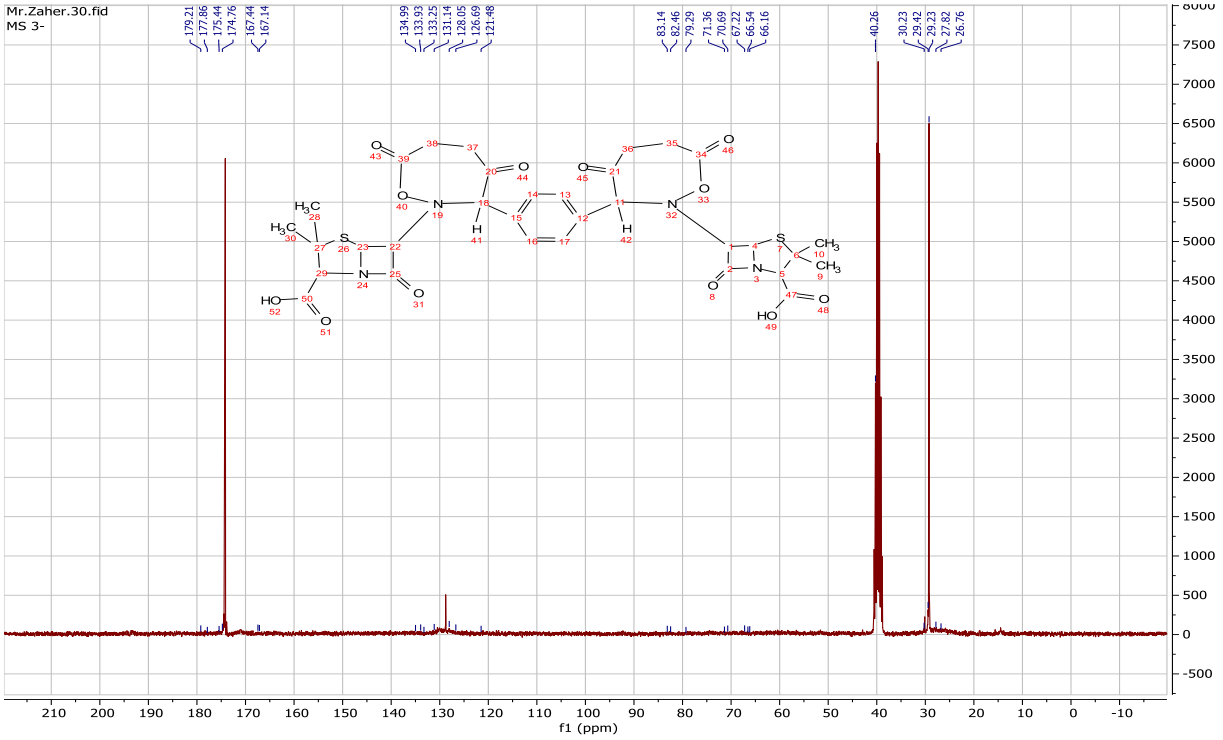


Fig. (3.80)^{13}CNMR Spectra of C4

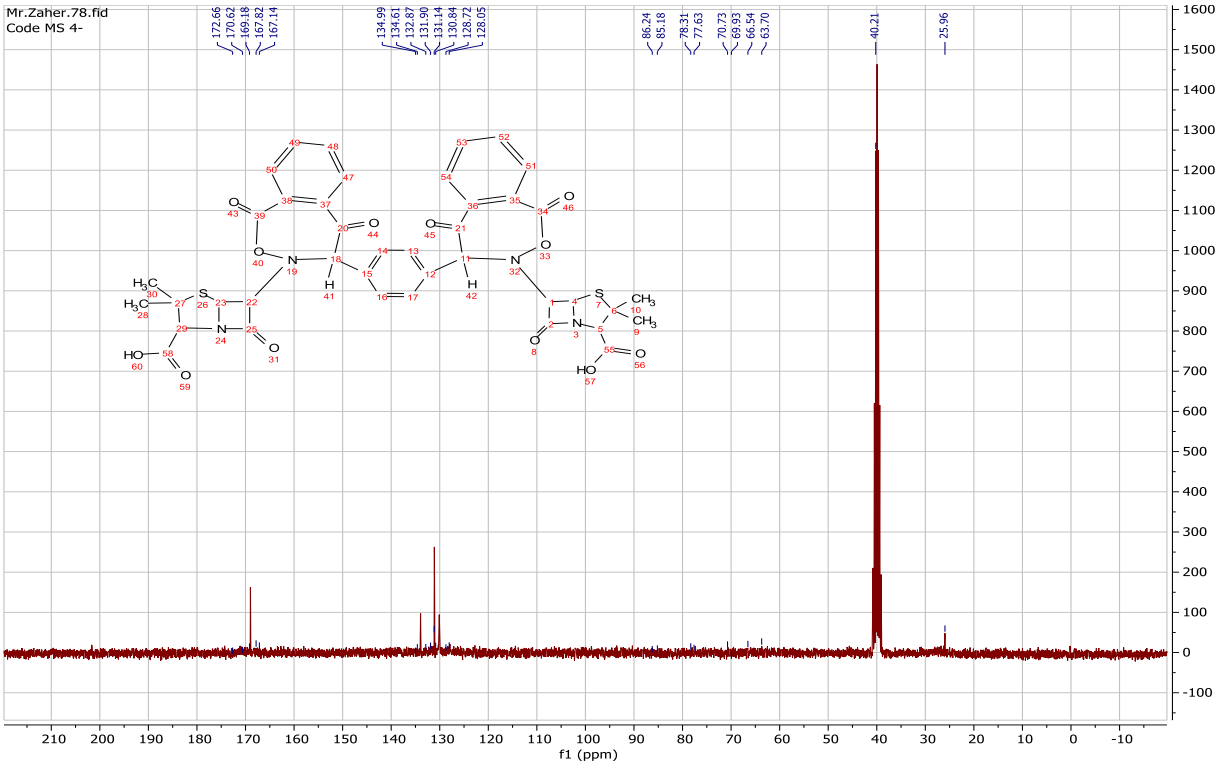


Fig. (3.81)^{13}CNMR Spectra of C5

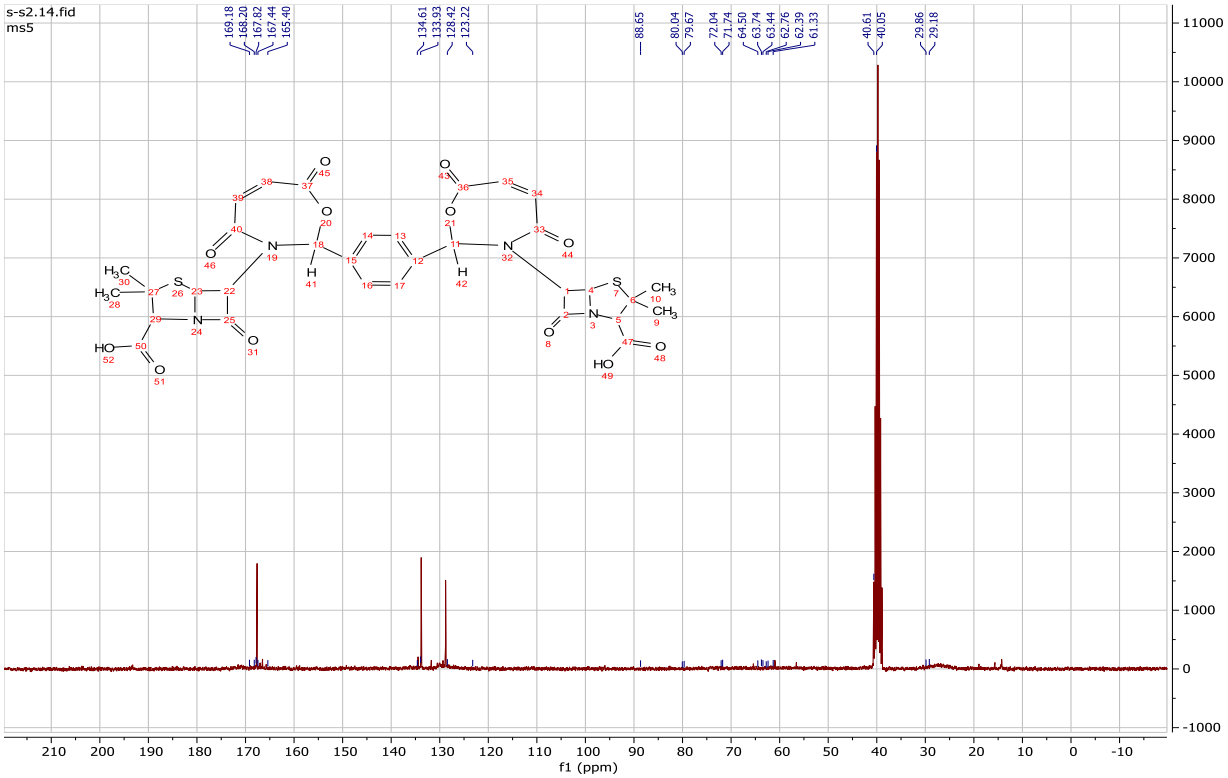


Fig. (3.82)^{13}CNMR Spectra of C6

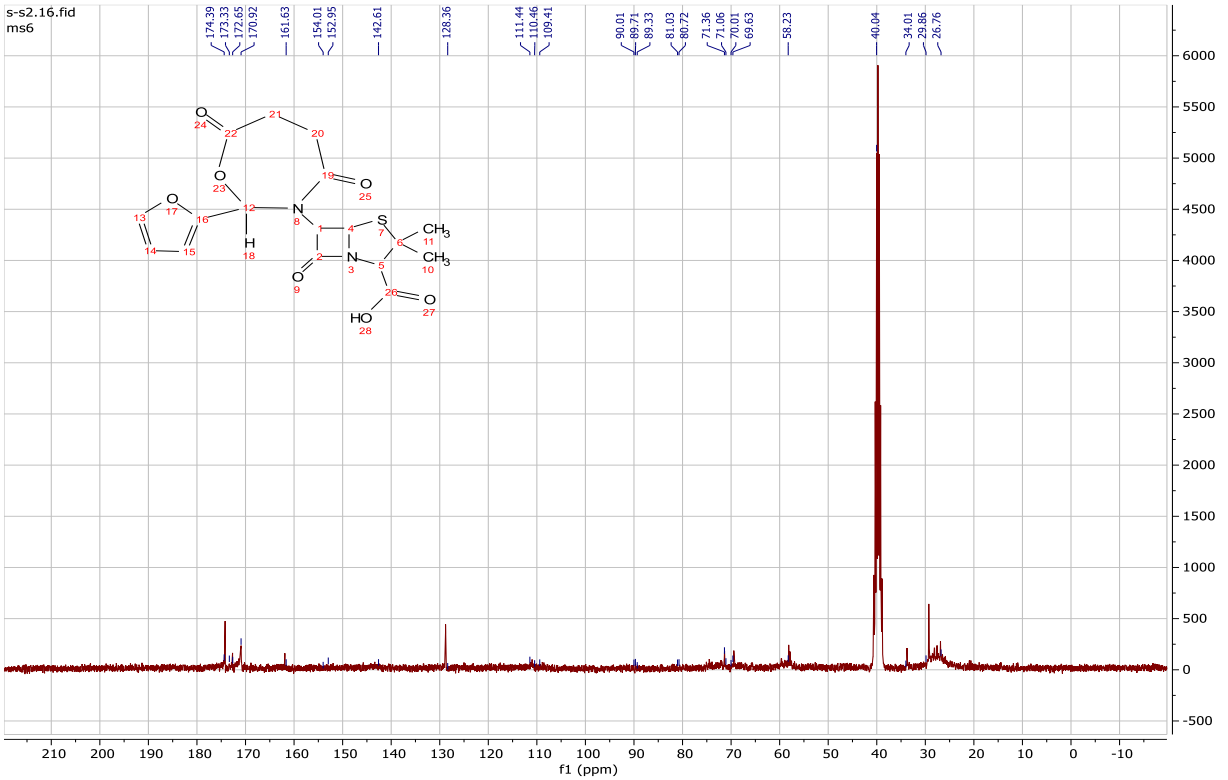


Fig. (3.83)^{13}CNMR Spectra of C7

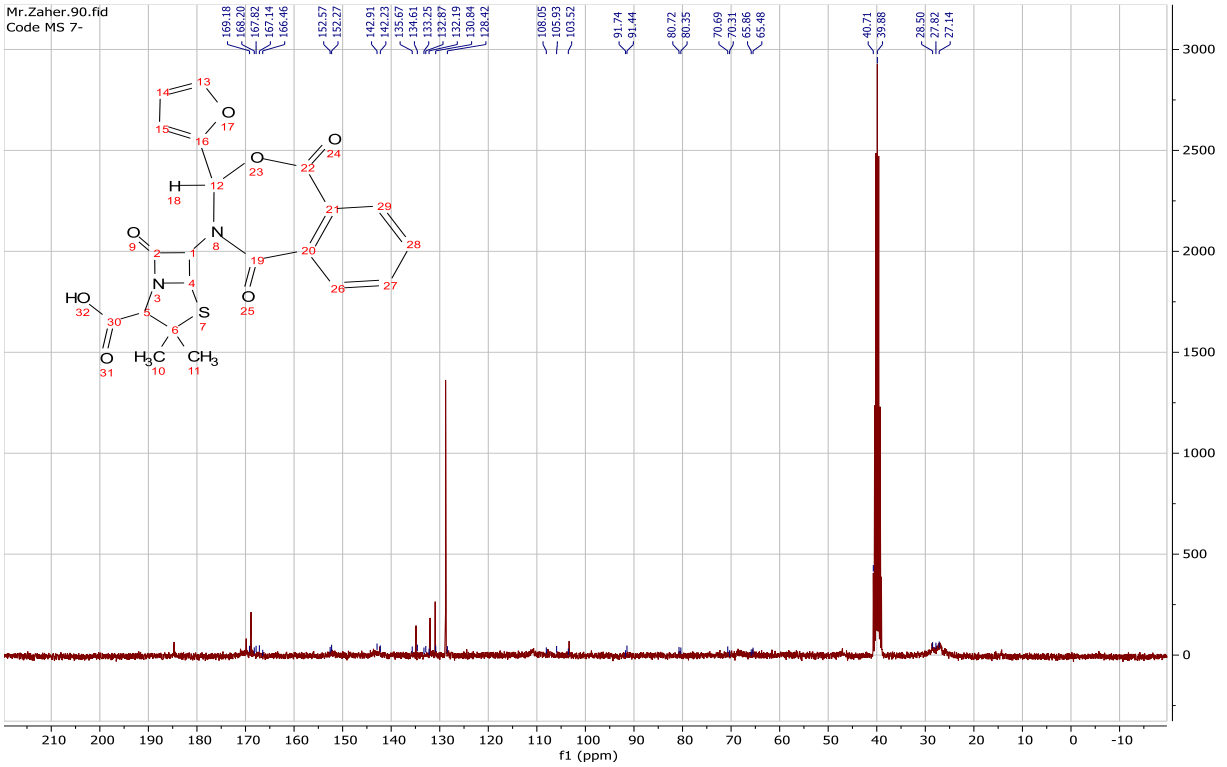


Fig. (3.84)^{13}CNMR Spectra of C8

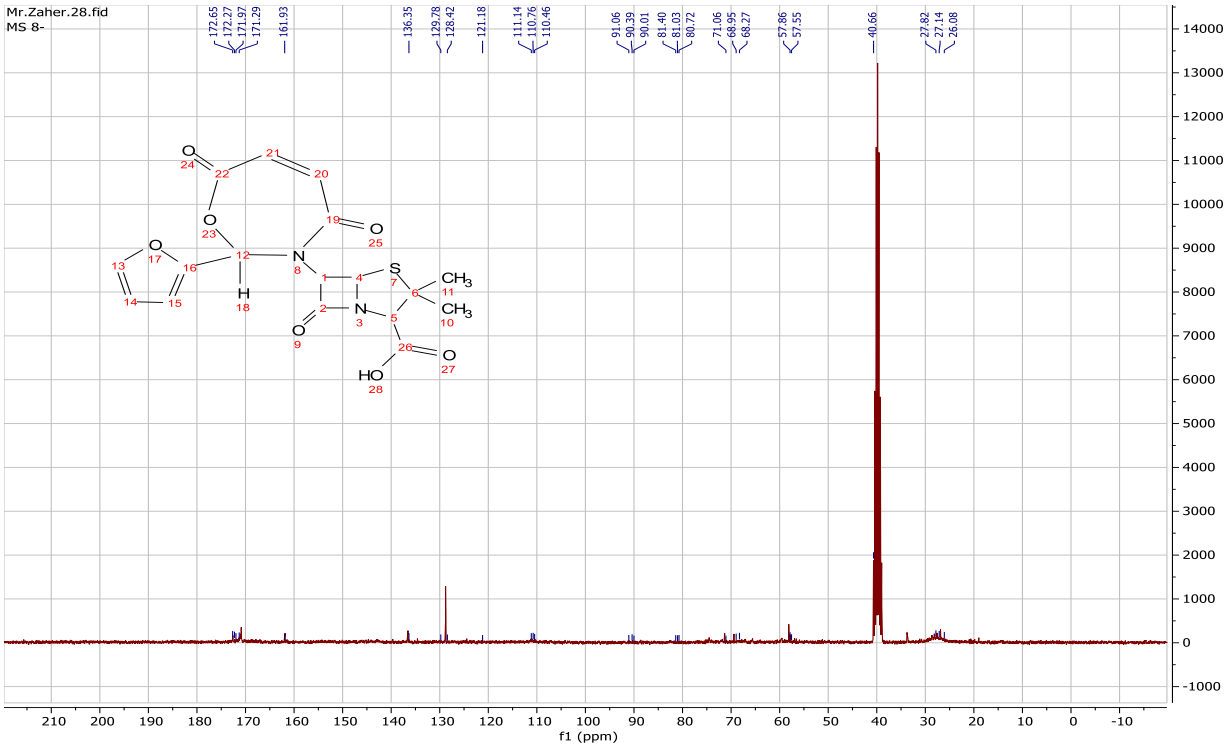


Fig. (3.85)^{13}CNMR Spectra of C9

3.22. U.V-visible absorption the prepared oxazepane's and their complexes:

The electronic spectra of the prepared oxazepane's (C1,C2,C3,C4,C5,C6,C7,C8,C9) were measured in the range(200-350) nm at room temperature using ethanol as a solvent [Waleed and AL-Hity, 2007]. The spectrum of the first the value (C1,C2,C3) (Fig.68,69,70) shows two absorption bands. The first bands belong to the transitions (π→π*) [Majed, Majid and Majed, 2018],while the second bands refers to the(n→π*). The spectrum of the oxazepane's (C4,C5,C6,C7,C8,C9) shows also three absorption bands in the range (200-400)nm. The first and the second bands refers to the(π→π*) transition, while the third one is related to the transition(n→π*). The spectrum of the complexes of oxazepane's (D1,D2,D3,D4,D5,D6,D7,D8,D9) shows also three absorption bands in the range (200-350)nm. The first and the second bands refers to the(π→π*) transition, while the third one is related to the transition(n→π*), which appears due to the presence of a double bond in addition to the presence of heterogeneous atoms in the it have ability to grant electronic pair and that confirm the coordination between the metal and the oxazepane's [Haddad, Yousif and Ahmed, 2013].

Table (3.11) Electronic spectra of the oxazepane's prepared and their complexes

Compound	Absorption Band ,λ nm	Transfers
C1	**208-234**	**π-π*, n-π***
C2	**206-228**	**π-π*, n-π***
C3	**211-228**	**π-π*, n-π***
C4	**212-255-314**	**π-π*, π-π*, n-π***

C5	**219-298-318**	**π-π*, π-π*, n-π***
C6	**222-259-312**	**π-π*, π-π*, n-π***
C7	**211-265-313**	**π-π*, π-π*, n-π***
C8	**209-267-314**	**π-π*, π-π*, n-π***
C9	**210-265-314**	**π-π*, π-π*, n-π***
D1	**215-274-315**	**π-π*, π-π*, n-π***
D2	**213-273-314**	**π-π*, π-π*, n-π***
D3	**222-271-315**	**π-π*, π-π*, n-π***
D4	**220-257-308**	**π-π*, π-π*, n-π***
D5	**221-281-311**	**π-π*, π-π*, n-π***
D6	**220-258-307**	**π-π*, π-π*, n-π***
D7	**211-263-309**	**π-π*, π-π*, n-π***
D8	**216-262-310**	**π-π*, π-π*, n-π***
D9	**212-262-309**	**π-π*, π-π*, n-π***

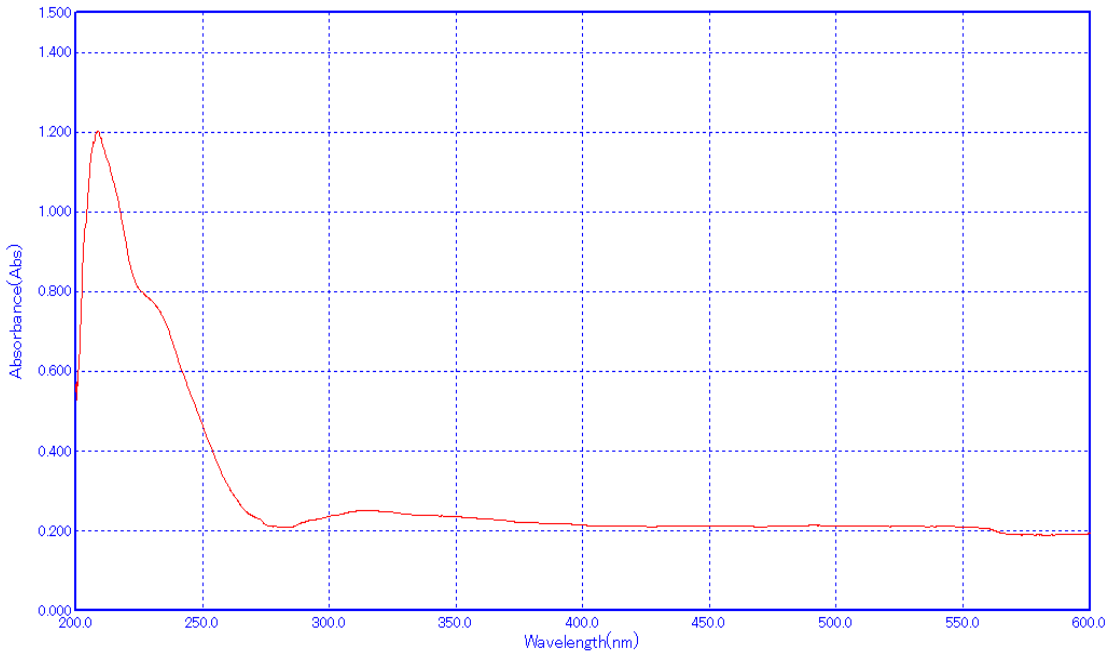


Fig. (3.86) UV-Vis spectrum of C1

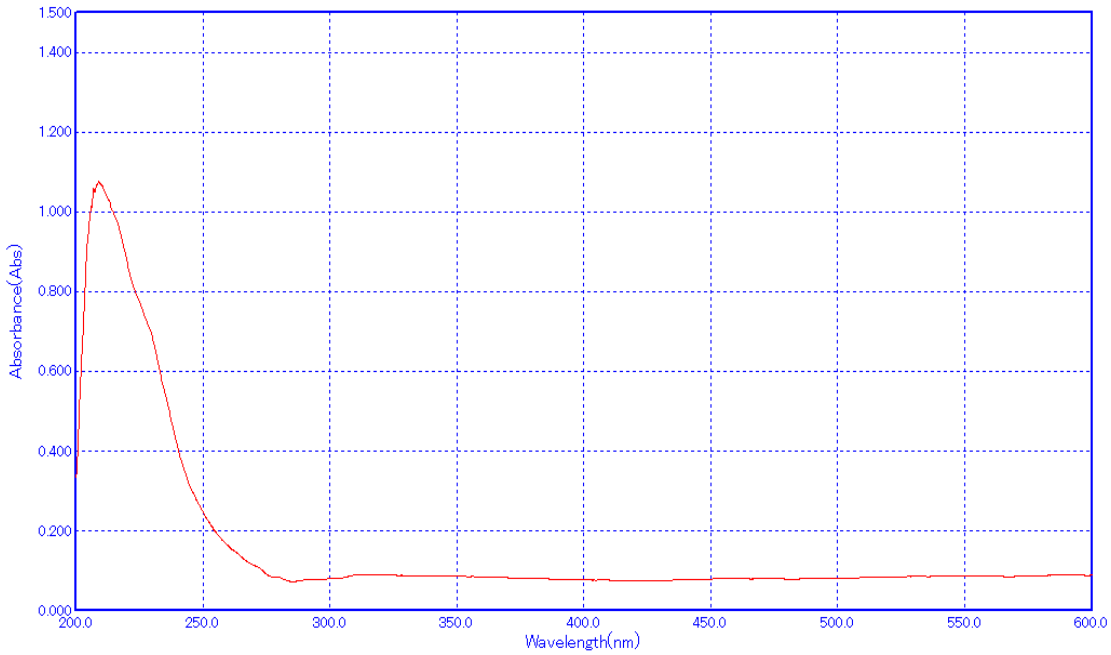


Fig. (3.87) UV-Vis spectrum of C2

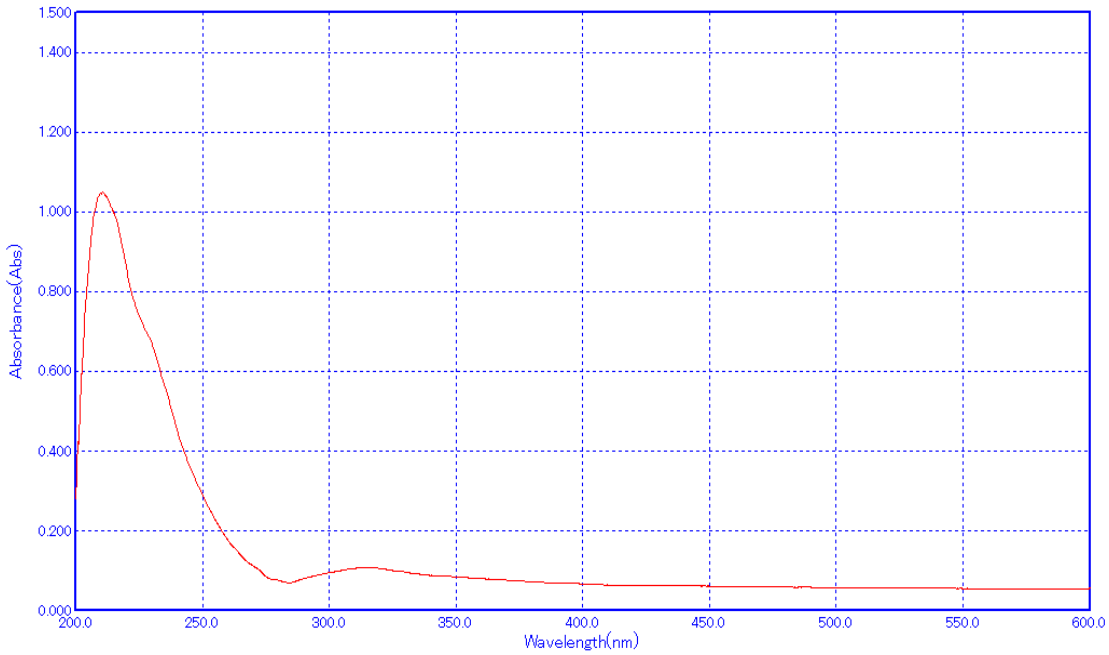


Fig. (3.88) UV-Vis spectrum of C3

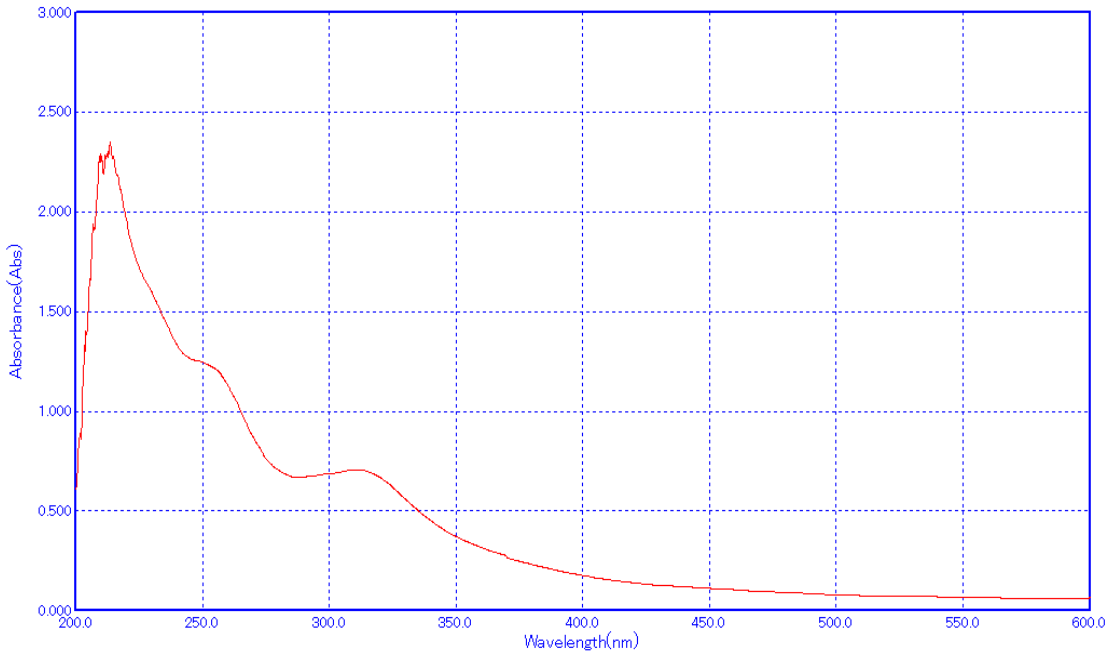


Fig. (3.89) UV-Vis spectrum of C4

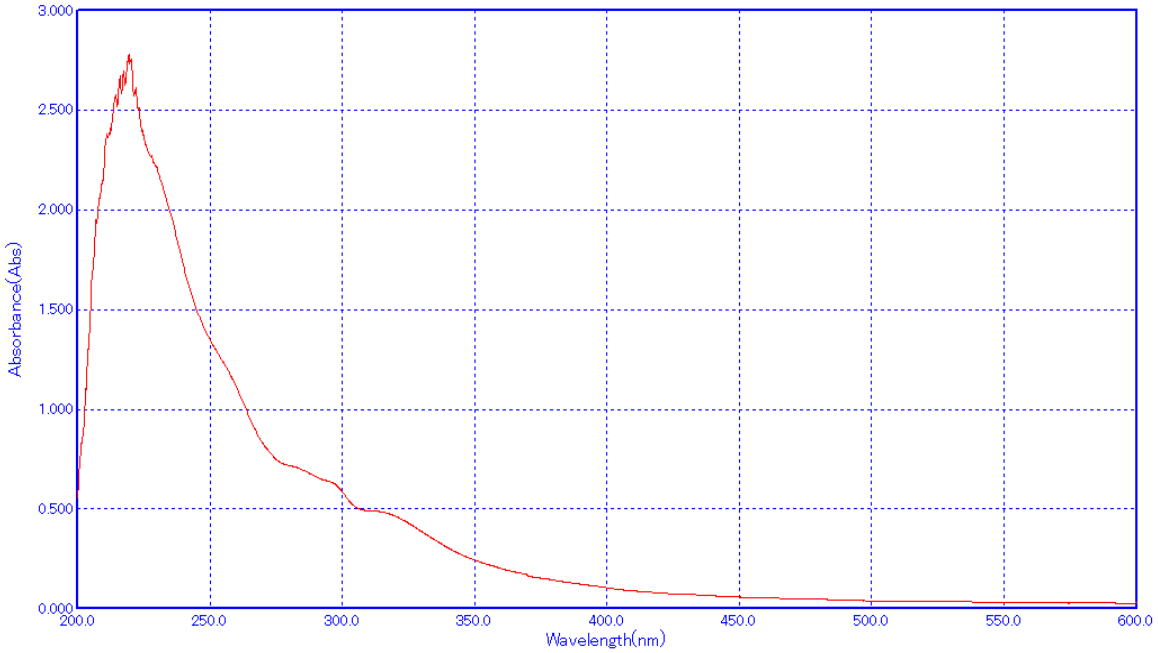


Fig. (3.90) UV-Vis spectrum of C5

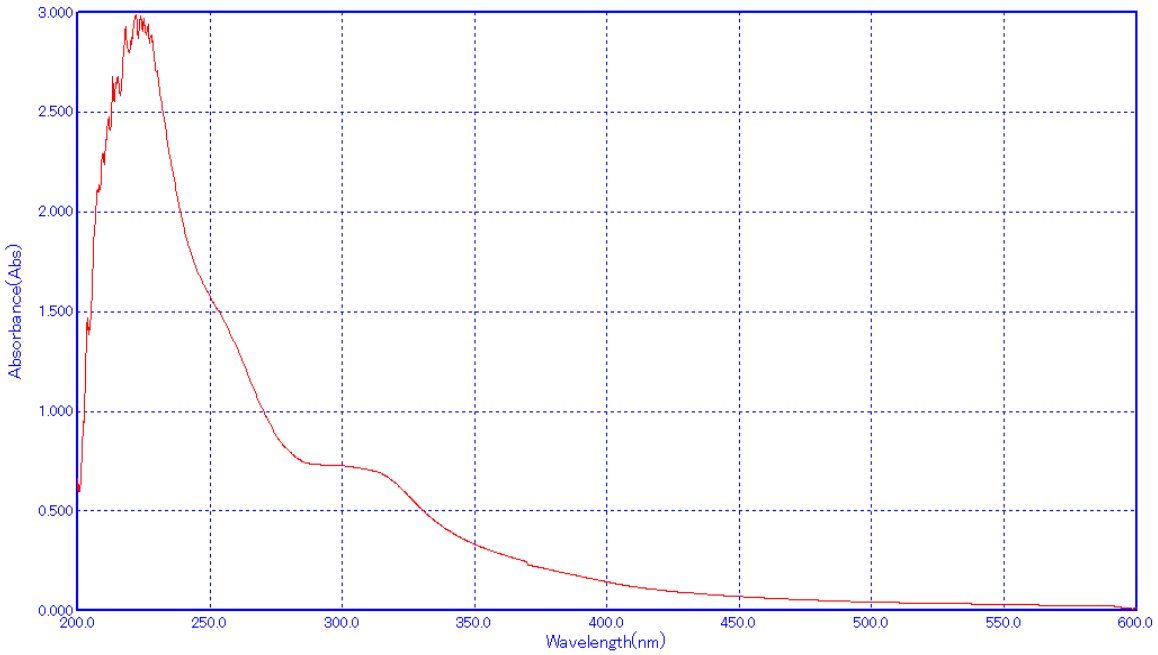


Fig. (3.91) UV-Vis spectrum of C6

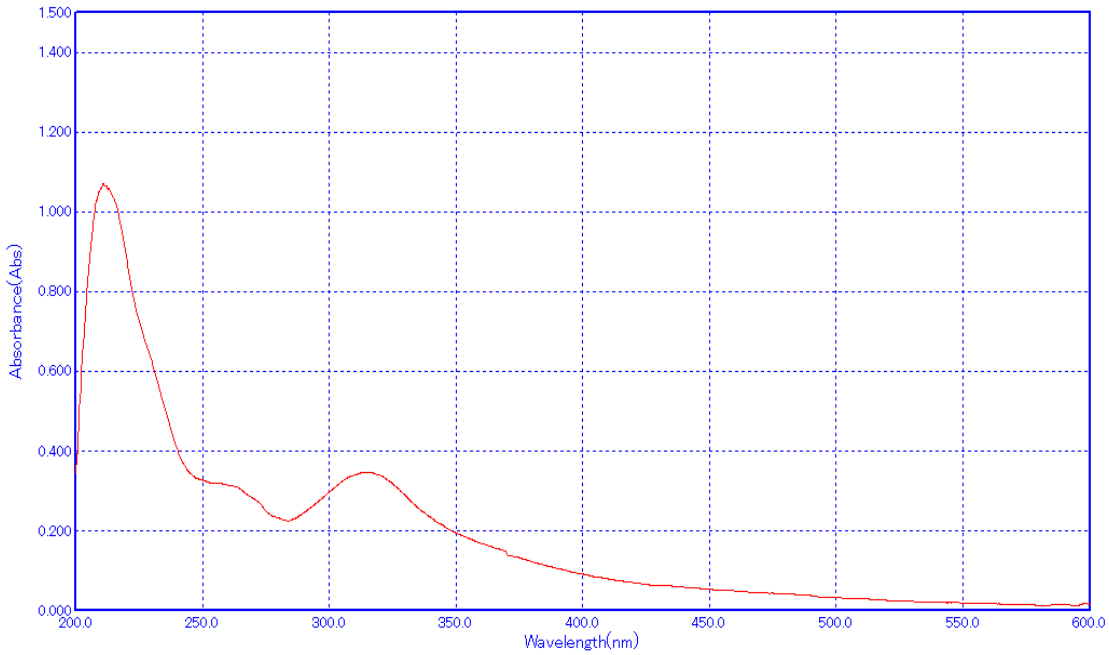


Fig. (3.92) UV-Vis spectrum of C7

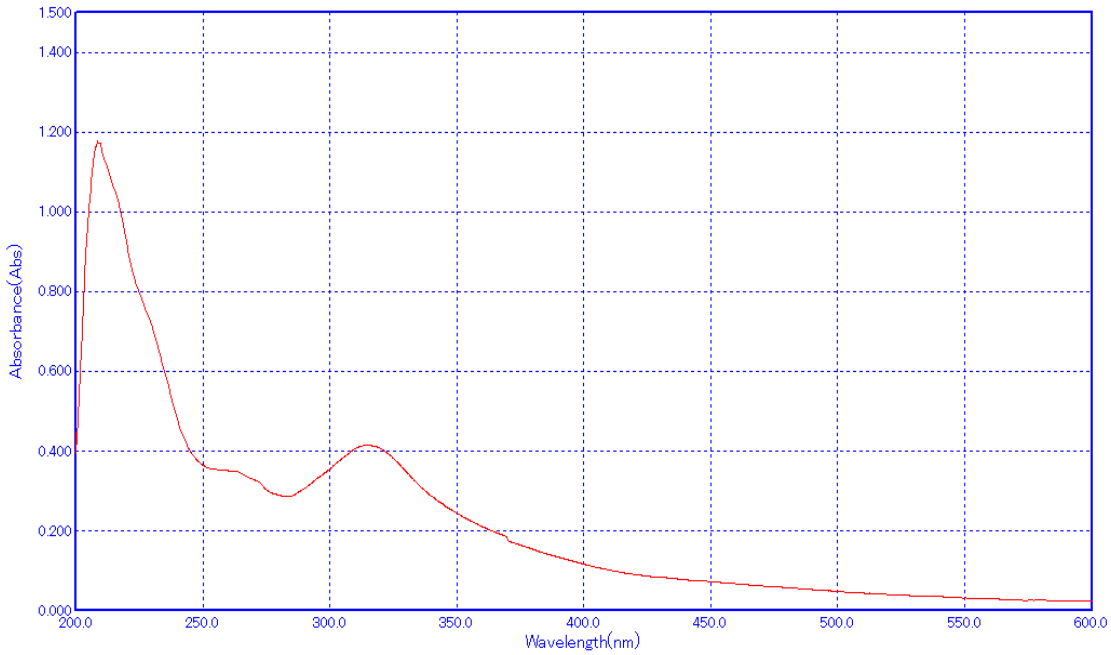


Fig. (3.93) UV-Vis spectrum of C8

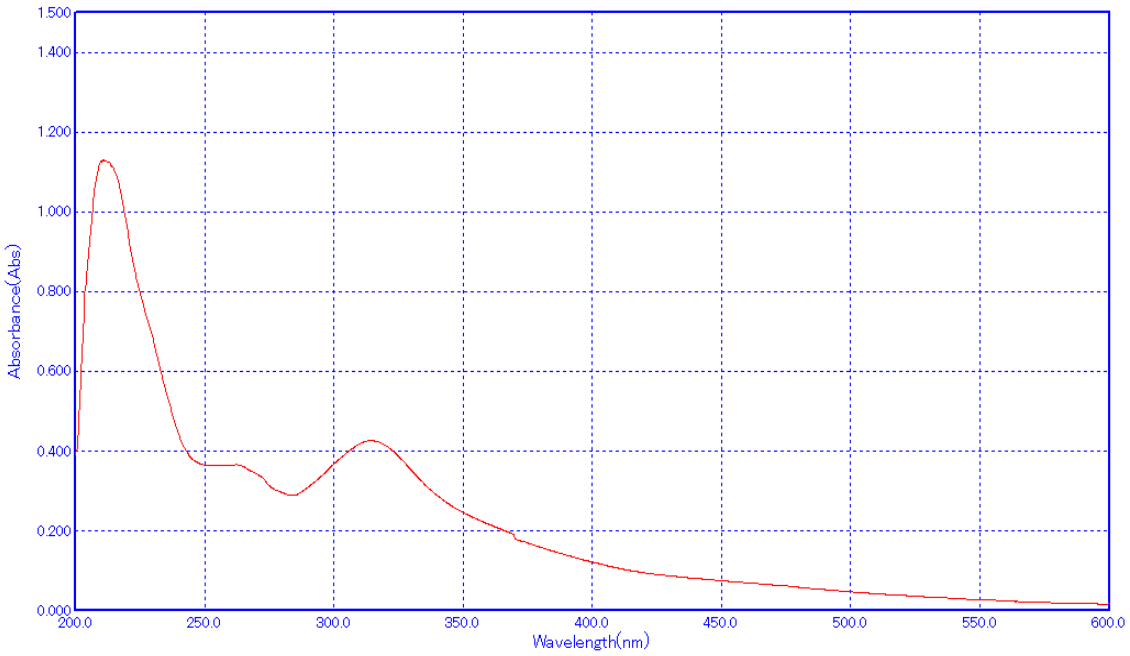


Fig. (3.94) UV-Vis spectrum of C9

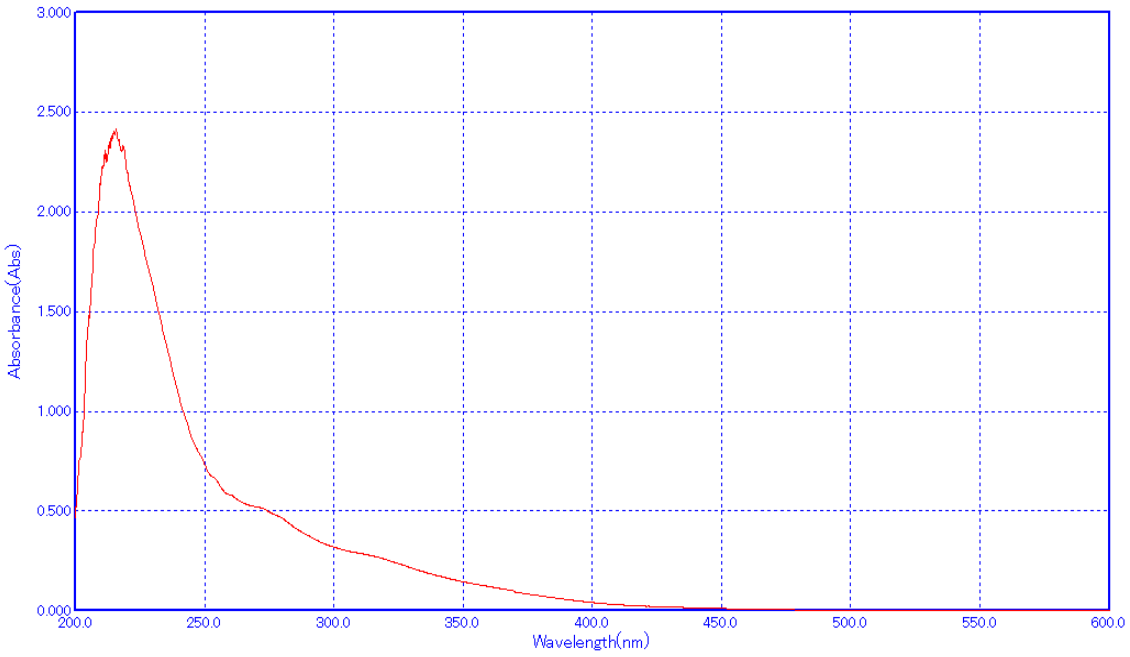


Fig. (3.95) UV-Vis spectrum of [D1]

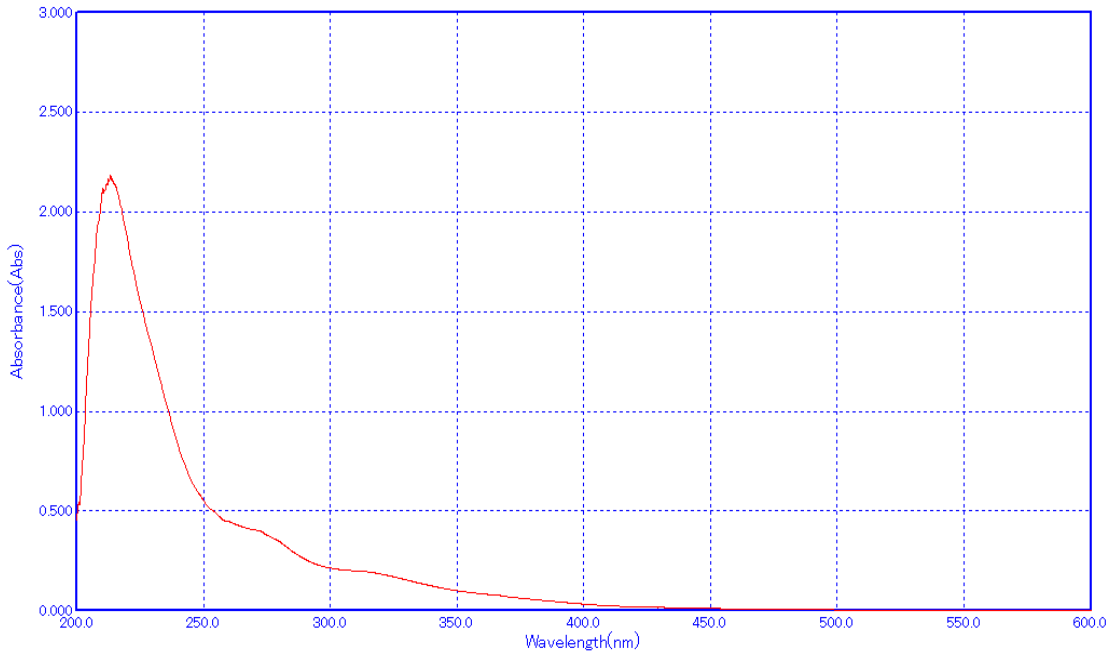


Fig. (3.96) UV-Vis spectrum of [D2]

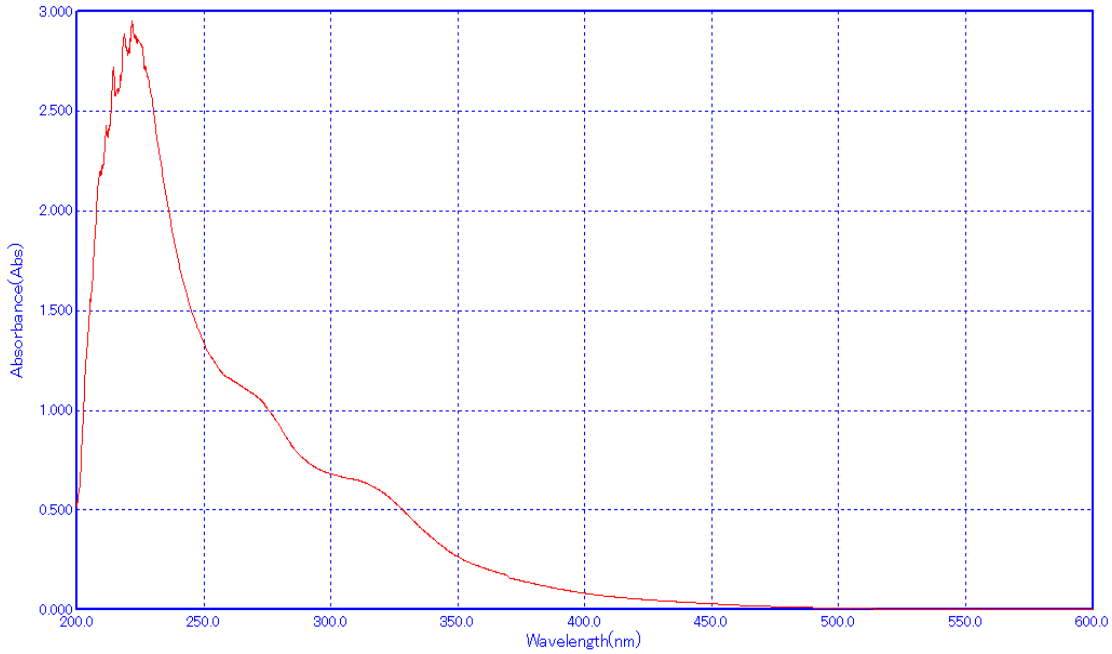


Fig. (3.97) UV-Vis spectrum of [D3]

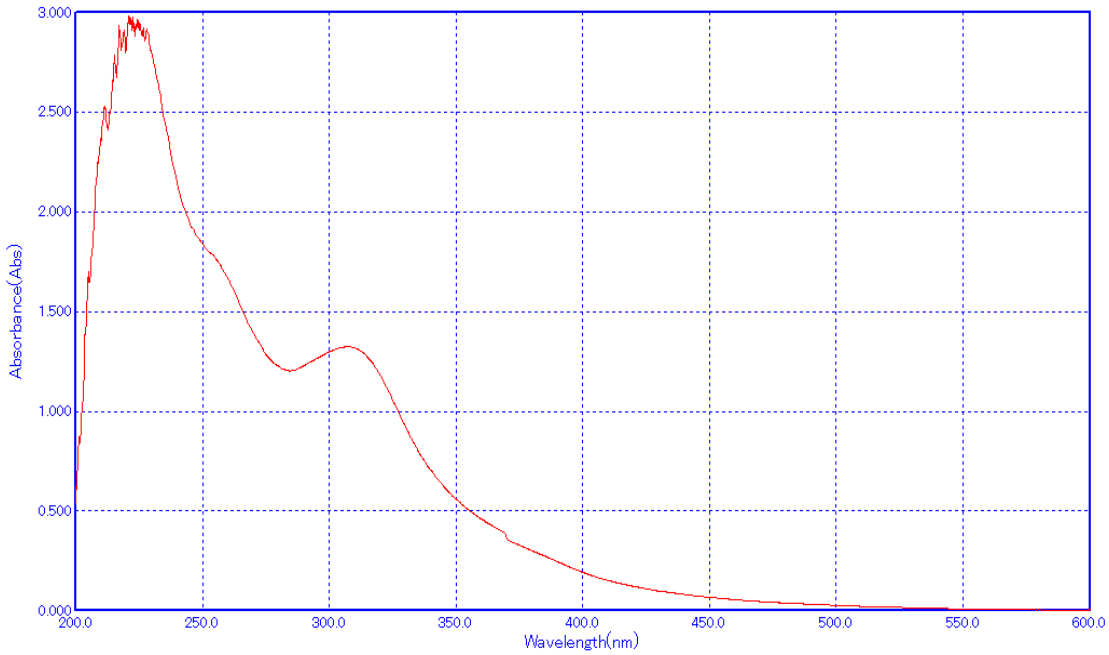


Fig. (3.98) UV-Vis spectrum of [D4]

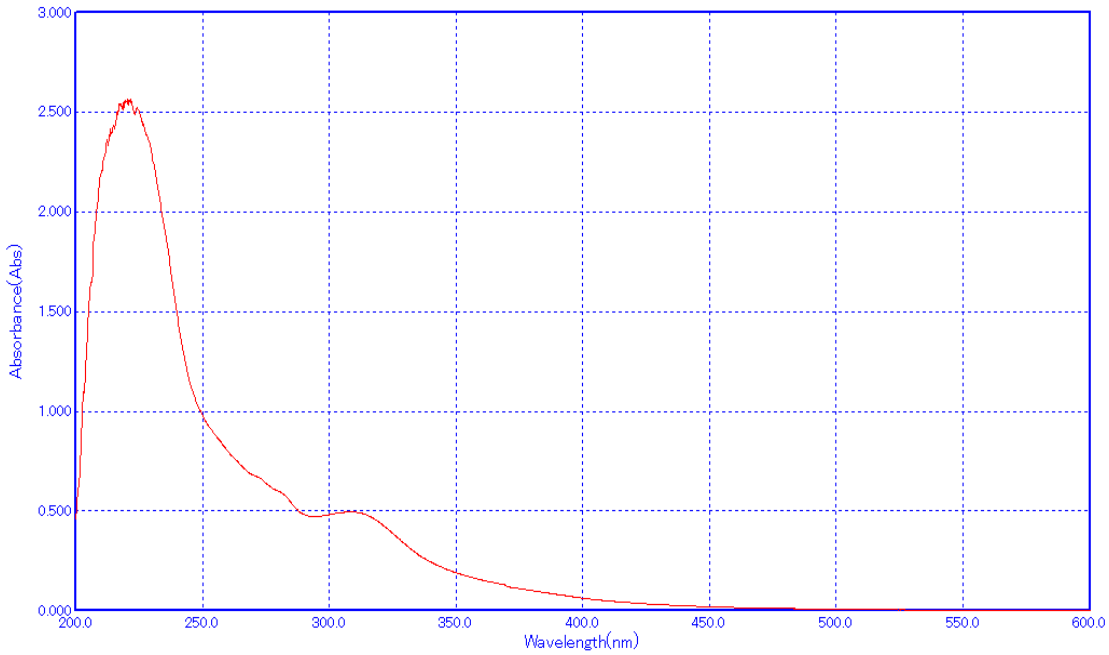


Fig. (3.99) UV-Vis spectrum of [D5]

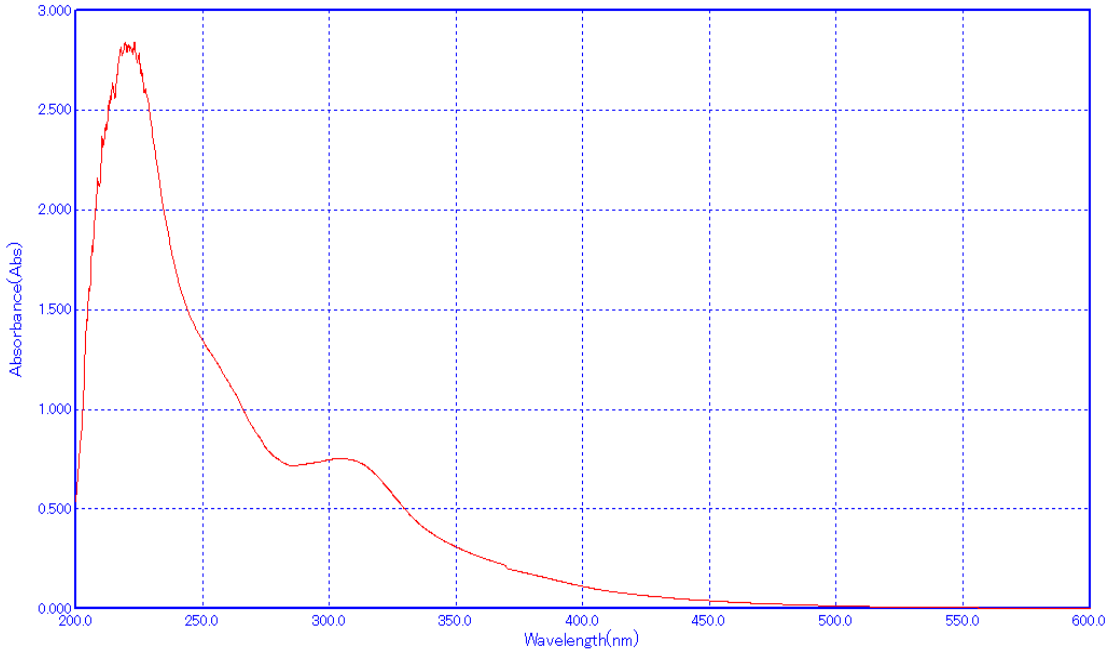


Fig. (3.100) UV-Vis spectrum of [D6]

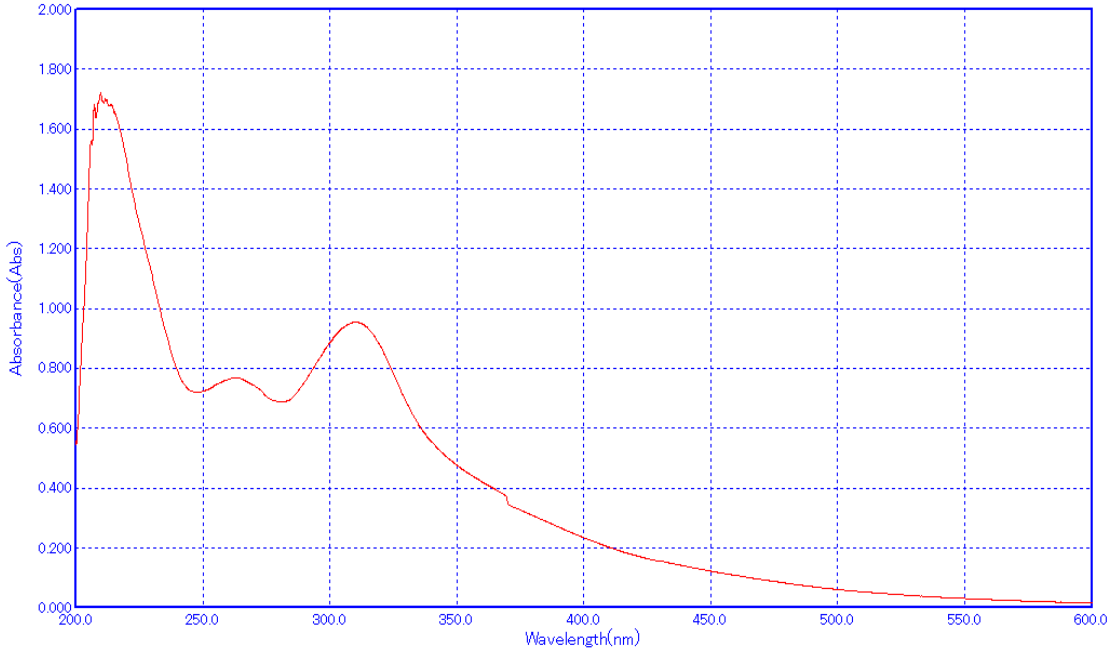


Fig. (3.101) UV-Vis spectrum of [D7]

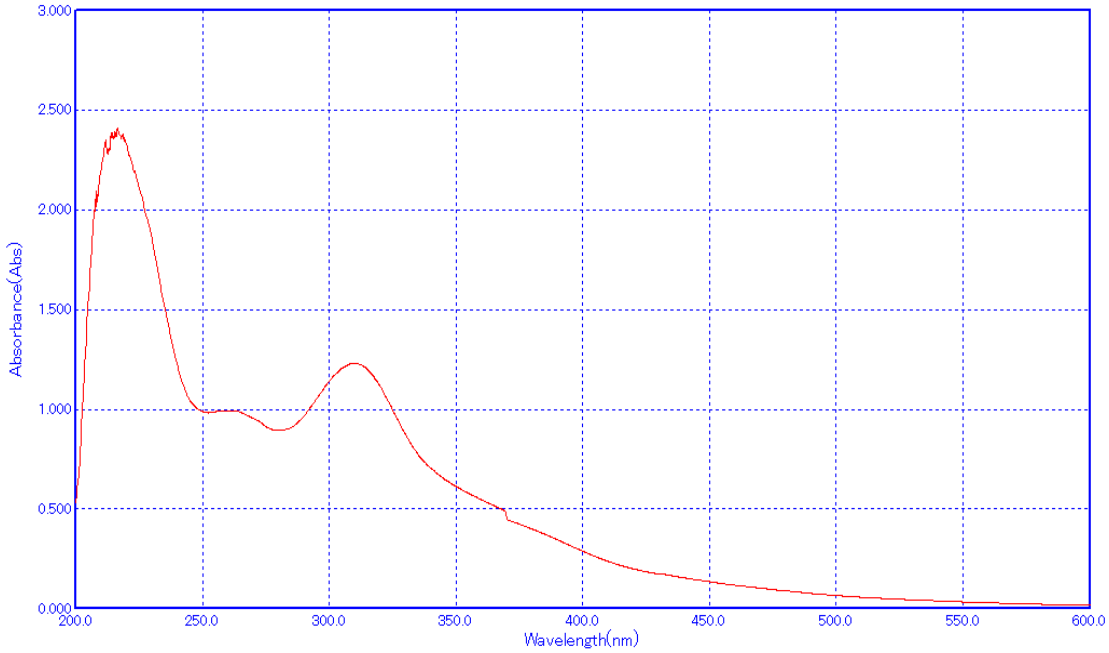


Fig. (3.102) UV-Vis spectrum of [D8]

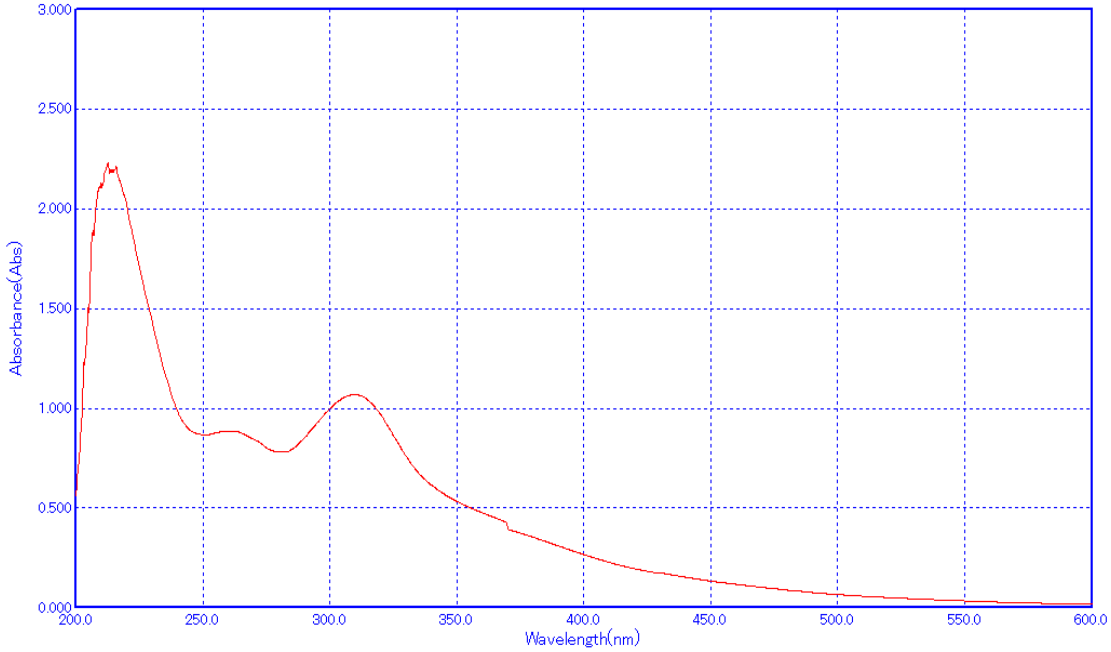


Fig. (3.103) UV-Vis spectrum of [D9]

3.23.Atomic absorption

The atomic absorption approach was used to calculate the percentage of zinc divalent ions in their complexes. The results reveal a good fit between the theoretical and practical values. In Furthermore, the findings confirm the complexes' hypothesized structure and type hybridization as shown in the table (3.11)

Table (3.12): Practical and theoretical values for the ratio of metals in the prepared complexes and type hybridization

complexes	*Theoretical value %*	*Practical value %*	*Suggested structure*	*hybridization*
D1	***7.47***	***7.13***	***Octahedral***	***sp^3d^2***
D4	***8.21***	***7.51***	***Octahedral***	***sp^3d^2***
D7	***7.65***	***6.52***	***Octahedral***	***sp^3d^2***

3.24.Molar conductivity

The molar conductivity of solutions is commonly used in coordination chemistry to determine the ionic formulae of compounds in solution, whether neutral or ionic. The higher the conductivity value, the more ions that are liberated in solution[Geary ,1971]. At room temperature, the molar conductance values of the synthesized complexes at a concentration of (10^{-3}M) and dissolved in Dimethyl sulfoxide [DMSO] as a solvent. Were included in the table (3-12). The data shown in this table demonstrated that the conductivity that appeared for complexes was of a non-electrolytic type[Maream *et.al.*,2021].

Table(3.13):The values of molar conductivity of complexes at($1*10^{-3}$) M in (DMSO):

Complexes	Molar conductivity ($Ohm^{-1}.mol^{-1}.cm^{-1}$)
$[Zn(C1)_2Cl_2]$	25.3
$[Zn(C2)_2Cl_2]$	24.4
$[Zn(C3)\ Cl_2]$	25.1
$[Zn(C4)\ Cl_2]$	15.7
$[Zn(C5)\ Cl_2]$	19.1
$[Zn(C6)\ Cl_2]$	13.6
$[Zn(C7)_2\ Cl_2]$	14.6
$[Zn(C8)_2\ Cl_2]$	15.7
$[Zn(C9)_2\ Cl_2]$	12.3

3.25. Study of biological activity

β-lactam antibiotics are extensively used across the world, including in Vietnam. β-lactams are used in medical treatment to boost antibacterial efficacy, either alone or in combination with another drug[Nguyen *et.al*., 2019].Schiff bases are an important class of chemical compounds with antiproliferative, antimalarial, antibacterial, antipyretic, antifungal, antiviral, and anti-inflammatory effects [Fadhil, Samir and Mahmood Rumez, 2016].

Oxazepine, which is synthesized via the pericyclic cycloaddition of [maleic, pthalic, and succinic] anhydrides with Schiff bases, has biological activity as (antagonistic, hypnotic muscle relaxant, anti-bacterial, telomerase inhibitors, antifungal, antiepileptic, and antiinflammatory)[Mohammad, Ahmed and Mahmoud, 2017], [Fadhil, Samir and Mahmood Rumez, 2016].

3.25.1.Prepared laboratory media:

Nutrient Agar Medium:

Nutrient agar medium has been prepared according to the manufacturing company. It has been used for general experiment isolate culture, cultivation and activation of bacterial isolates when it is necessary [McFadden, 2000].

3.25.1.1.Brain Heart Infusion Agar:

Brain-heart infusion agar was prepared according to the manufacturing company. The medium was autoclaved at (121ºC) for (15) minutes and used for detection of different biochemical tests [McFadden, 2000].

3.25.1.2.Mullar- Henton Agar:

Mullar–Henton agar were formed using prescribed ways (McFadden, 2000), in which 38gm was dissolved liter of distilled water with used antimicrobial susceptibility research.

3.25.2.McFarland Turbidity Standard

It was prepared by mixing 0.5 ml of 1.175% (W/V) barium chloride dihydrate ($BaCl_2.2H_2O$) solution with 99.5 ml of 1% (V/V) sulfuric acid (H_2SO_4). Then the McFarland standard solution was transferred to screw capped tube and sealed tightly, then covered with aluminum foil to protect it from light and stored in a dark place at room temperature. The accuracy of the density of the prepared 0.5 McFarland standard was checked by a spectrophotometer at 625 nm to give a value of 0.08- 0.13. In microbiology, McFarland standard is utilized as a reference to adjust the turbidity of bacterial suspension with 0.5 McFarland standard solutions which should be equivalent to 1.5×10^8 CFU/ml [CLSI, 2021].

3.25.3.Study the effect of Ligand and Complexes as antibacterial activity by using Well-Diffusion Assay (WDA)

1- Bacterial isolate (*Pseudomonas and Staphylococcus aureus*) was activated overnight in Brain heart infusion broth at 37 ºC.
2- Culture was washed twice with sterile normal saline then centrifuged at 12000 rpm for 10 min and re suspended in normal slain. The turbidity of suspension was adjusted to 0.5 McFarland in to prepare the inoculums.
3- A sterile swab was used to obtain an inoculum from the bacterial suspension. These inoculums were streaked on a Mueller-Hinton agar plate and left to dry.
4- Wells cut into the plates with 5mm sterile cork borer were loaded with 100 µl of the Ligand and Complexes.
5- Inhibition zones were measured using a ruler and compared with the zones of inhibition determined by the original material.

Table(3.14) Biological activity for the ligand and complexes

Compound	**Number**	***Staphylococcus aureus***	***Pseudomonas***
L1	**1**	***2.8 cm***	***1.9 cm***
L2	**2**	***2.9 cm***	***1.8 cm***
L3	**3**	***2.5 cm***	***2 cm***
L4	**4**	***3.1 cm***	***1.5 cm***
$[Zn(L1)_2Cl2]$	**5**	***2.3 cm***	***2.1 cm***
$[Zn(L2)_2Cl2]$	**6**	***2.1 cm***	***1.6 cm***

[Zn(L3)$_2$Cl2]	**7**	***2.4 cm***	***1.5 cm***
[Zn(L4)$_2$Cl2]	**8**	***2.8 cm***	***2.6 cm***

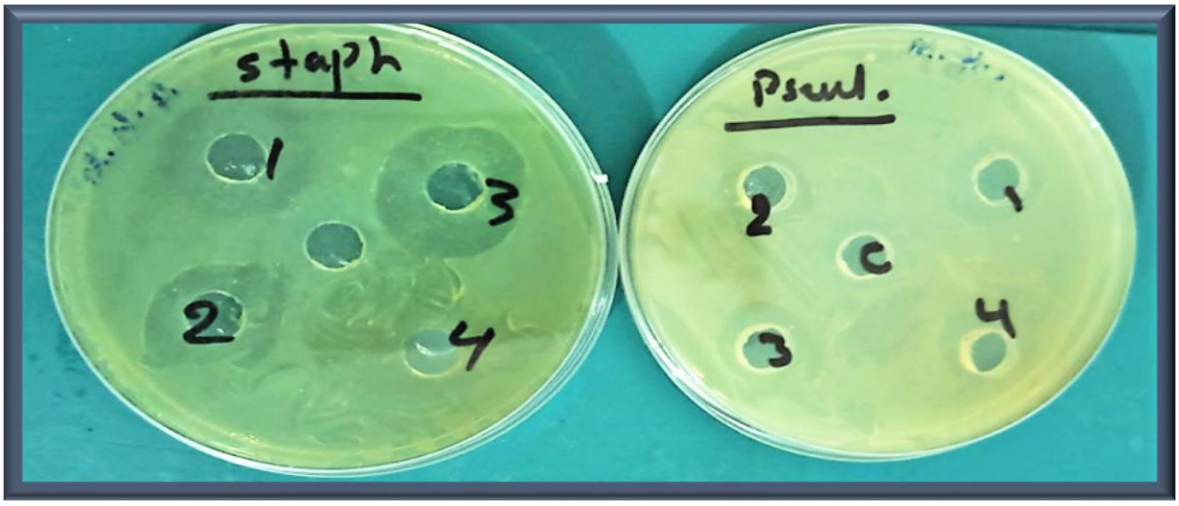


Fig (104) The Effect of a Compound(L1,L2,L3,L4) on staph. and pseud.

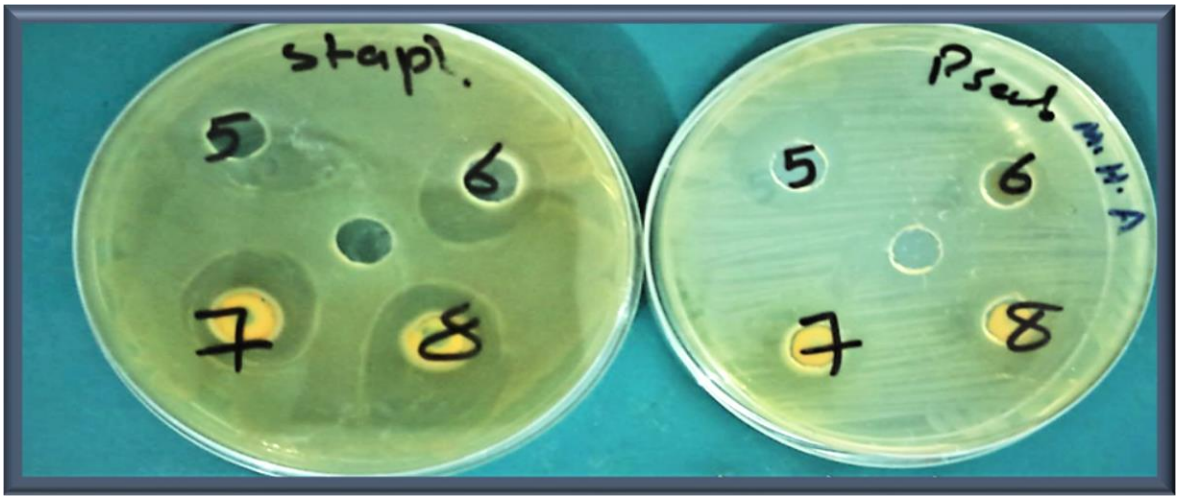


Fig (105) The Effect of a Compound(B1,B2,B3,B4) on staph. and pseud.

Table(3.15) Biological activity for the oxazepane's and complexes

Compound	*Number*	*Staphylococcus aureus*	*Pseudomonas*
C1	9	2.7 cm	1.7 cm
C2	10	3.1 cm	2.4 cm
C3	11	3.4 cm	2.1 cm
C4	12	2.6 cm	2 cm
C5	13	2.2 cm	1.7 cm
C6	14	2.7 cm	2.1 cm
C7	15	2.9 cm	2.3 cm
C8	16	2.7 cm	2.1 cm
C9	17	2.8 cm	
D1	18	3.7 cm	
D2	19	1.9 cm	
D3	20	2.7 cm	
D4	21	2.1 cm	
D5	22	2.6 cm	
D6	23	3.1 cm	
D7	24	1.4 cm	
D8	25	2.8 cm	
D9	26	3.1 cm	
6-APA	A	1.5 cm	1.3 cm
DMSO	D	1.3 cm	1.1 cm

Fig (106) The Effect of a Compound(C1,C2,C3,C4,DMSO) on staph. and pseud.

Fig (107) The Effect of a Compound(C5,C6,C7,C8,6-APA) on staph. and pseud.

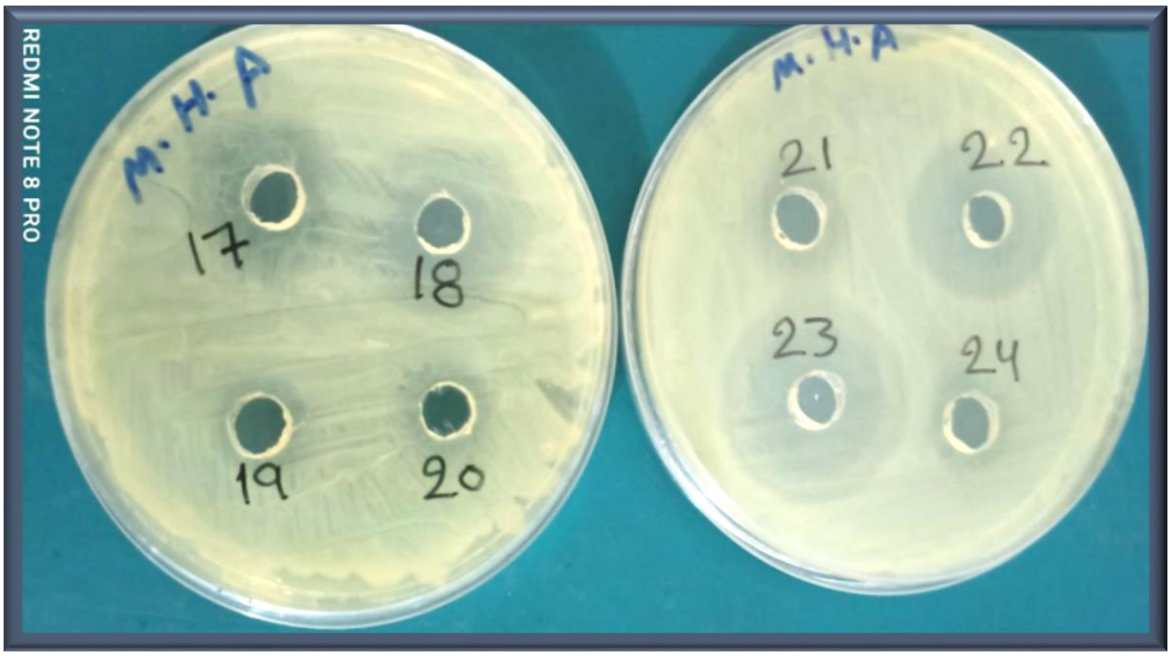


Fig (108) The Effect of a Compound(C9,D1,D2,D3,D4,D5,D6,D7,) on staph.

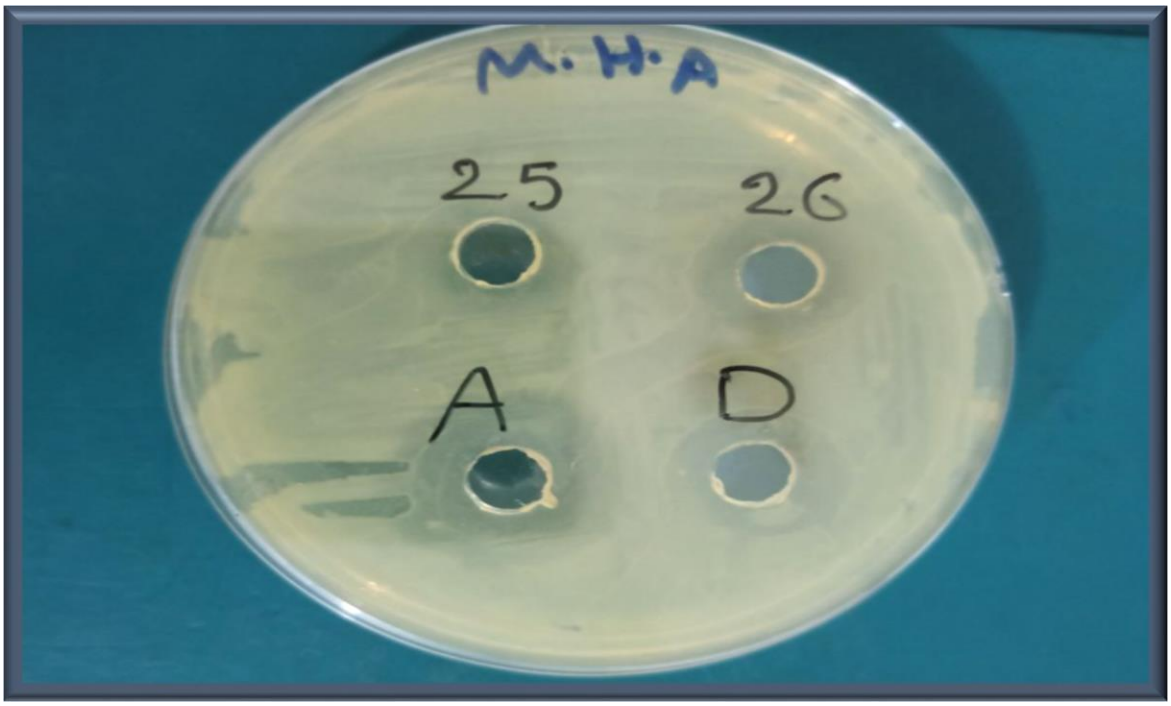


Fig (109) The Effect of a Compound(D8,D9,6-APA,DMSO) on staph.

3.26 Conclusions:

1. In this study, four types of ligands (L1, L2, L3, and L4) and four complexes (B1, B2, B3 and B4) of transition metal Ion Zn (II) were synthesized in the high yield.

2. In this study, nine types of 1,3-oxazepine derivatives (C1, C2, C3, C4, C5, C6, C7, C8 and C9) and nine complexes (D1, D2, D3, D4, D5, D6, D7, D8 and D9) of transition metal Ion Zn (II) were synthesized in the high yield.

3. These ligands and 1,3-oxazepine derivatives were confirmed by the following assays (FT-IR, ^{13}C-NMR, ^{1}H-NMR and Mass Spectra).

4. The mole ratios [M: L] were [1:2], except (L3) the mole ratio [M: L] were [1:1].

5. According to the conductivity values, all complexes are non-electrolytes.

6. The structure of the synthesized complexes was supposed to be octahedral.

7. The biological activity of ligands and complexes was studied; ligands and the complexes; 1,3-oxazepine derivatives and the complexes, demonstrated the potential to inhibit against two types of bacteria (*Pseudomonas and Staphylococcus aureus*), the biological activity of the prepared ligands and complexes against bacteria (*Staphylococcus aureus*) is more effective than that of bacteria (*Pseudomonas*).

8. The beta-lactam ring remains unbroken.

3.27 Suggestions for future works

1. Synthesis of new Schiff bases derivatives using different aldehydes with primary amines.

2. Synthesis of new sets of complexes for all ligands using other sets of metal ions.

3. Synthesis of new 1,3-oxazepine derivatives using different anhydrides with ligands.

4. Evaluation of the antibacterial activity of synthesized compounds in vitro against different types of bacteria.

5. Conducting further biological studies on the prepared compounds, in vivo studying of interaction with various biological systems

6. Testing the efficacy of 1,3-oxazapine derivatives as anticancer, epilepsy and psychological disorders.

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الخلاصة

تم تحضير خمسة ليكاندات عن طريق تفاعل 6-aminopenicillanic acid (6-APA) مع(Benzaldehyde،Terephthalaldehyde،Crotonealdehyde،n-Butylaldehyde Furfuraldehyde,) لإنتاج(L1، L2، L3، L4, L5)على التوالي. تم تحضير أربعة معقدات جديدة من خلال تفاعل الليكاندات المشتقة أعلاه مع أيونات المعدن(II) Zn ، حيث تفاعل L1 و L2 وL4 مع أيونات المعدن هذه في نسبة [1: 2] معدن إلى ليكاند[M: L] على التوالي ، ولكنL3 في نسبة [1: 1] معدن إلى ليكاند.

وفي هذا العمل أيضا تم تحضير مشتقات 1،3-أوكسازيبين عن طريق تفاعل قواعد شيف مع (Succinic anhydride، phthalic anhydride and malic anhydride) لإعطاء مشتقات الحلقة الحلقية غير المتجانسة المكونة من سبع ذرات لإنتاج (C1,C2,C3,C4,C5,C6,C7,C8,C9) وبواسطة مفاعلتها مع ايونات معدن الزنك تنتج تسع معقدات جديدة (D1,D2,D3,D4,D5,D6,D7,D8,D9) تم تشخيص المركبات المحضرة بواسطة FT- IR، (H^1 وC^{13}) مطيافية الرنين المغناطيسي النووي ، الامتصاص الذري ، مقياس الطيف الكتلي ، تم فحص المركبات المحضرة لنشاطها المضاد للبكتيريا ضد البكتيريا (السالبة والموجبة) وتم اكتشاف أن قواعد شيف ، ومشتقات أوكسازيبين ومجمعاتها مثبط ممتاز ضد البكتيريا (الزائفة والمكورات العنقودية الذهبية). نتيجة لذلك، قد تكون المركبات المطورة بدائل قابلة للتطبيق للأدوية شائعة الاستخدام.

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة بابل/ كلية العلوم للبنات
قسم الكيمياء

تحضير وتشخيص 1,3-اوكسازيبين 4,7-دايون عن طريق قواعد شف المحضرة من 6-امينو حامض البنسليك وقدرتها على الارتباط

رسالة

مقدمة الى مجلس كلية العلوم للبنات-جامعة بابل

من متطلبات نيل شهادة الماجستير في العلوم / علوم الكيمياء

من قبل

ميس سعيد عبيد

إشراف

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